

UNIVERSITY OF KWAZULU-NATAL

**THE COST-EFFECTIVENESS OF HIV/AIDS INTERVENTIONS IN
SOUTH AFRICA**

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Doctor of Philosophy in Economics**

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College of Law and Management Studies**

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DECLARATION

I, **Josué Mbonigaba**, declare that:

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From this thesis, one paper, "The Cost-Effectiveness of Intervening in Low and High HIV Prevalence Areas in South Africa", was developed and presented at two international conferences: 1) *The First International HIV Social Sciences and Humanities Conference on Locating the Social*, Durban 11-13 June 2011, and 2) *The 4th Annual International Society for Pharmacoeconomics and Outcome Research (ISPOR) Congress*, Johannesburg 5-6 October 2011. This paper, related to Chapter 7 of the thesis, was published as an Economic Research Southern Africa (ERSA) working paper no 304 in 2012 and; subsequently in 2013, in the *South African Journal of Economics and Management Sciences* 16(2): 183-198 in the same year.

A paper entitled "Modelling the Cost-effectiveness of HIV/AIDS Interventions in Different Socio-Economic Contexts in South Africa", also developed from the thesis was accepted for publication in the conference proceedings of *The 3rd International Conference on Qualitative and Quantitative Economics*, Bangkok, 20-21 May 2013. It was subsequently withdrawn from the conference proceedings in order to be published in the *Mediterranean Journal of Social Sciences*, 2(4): 587-600.

Furthermore, a paper entitled “The Case for the Cost-effectiveness Analysis of Contextual HIV/AIDS Interventions and the Extent to which it is Relevant to South Africa” was also developed from the thesis’s chapter 5. This paper was also published in the *Mediterranean Journal of Social Sciences* 4 (3): 743-752 in 2013.

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ABSTRACT

Despite some evidence that the effectiveness of HIV/AIDS interventions depends on the context of their implementation, there is a paucity of evidence on the cost-effectiveness (CE) of these interventions in South Africa. The objective of this study is therefore to compare the CE of major HIV/AIDS interventions in epidemiological and socio-economic contexts in South Africa using a methodology which takes into account the effect of the interaction between the context and HIV/AIDS interventions on the costs and effectiveness of such interventions. In epidemiological contexts, the CE of HIV/AIDS interventions is compared across a low HIV prevalence context (LPC) and a high HIV prevalence context (HPC) while in socio-economic contexts the comparison is done across a rural context and an urban context.

The comparison of the CE of HIV/AIDS interventions requires the follow-up of patients in HIV/AIDS progression states (non-infected, infected, AIDS, death) over time. However because this follow-up is costly, the thesis models hypothetical populations of HIV/AIDS patients in each context, using two types of models, namely, Markov models and population projection models. These models simulate and project patients in the above-mentioned HIV/AIDS states over time and the cost and effectiveness data, systematically collected from South African literature, are applied to simulated and projected patients.

The study finds that in epidemiological contexts, modelled HIV/AIDS interventions are generally more cost-effective in a LPC than they are in a HPC. In socio-economic contexts, the pattern of the CE of modelled HIV/AIDS interventions across a rural and an urban context is not specific and depends on the type of intervention. Prevention of mother-to-child transmission (PMTCT) is more cost-effective in the rural context than it is in the urban context while highly active antiretroviral treatment for adults and children is more cost-effective in the urban context than it is in the rural context. The study also finds that the extent of CE varies across HIV/AIDS interventions in any context. Therefore policy makers should allocate resources in accordance with these CE variations.

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LIST OF ACRONYMS

ACER:	Average cost-effectiveness ratio
AIDS:	Acquired immune-deficiency syndrome
ASSA:	Actuarial Society of South Africa
AZT:	Zidovudine
CE:	Cost-effectiveness
CEA:	Cost-effectiveness analysis
CEPAC:	Cost-effectiveness of preventing AIDS complications
DH:	Department of Health
EC:	Eastern Cape
FS:	Free State
G:	Gauteng
HAART:	Highly active antiretroviral
HIV:	Human immuno-deficiency virus
HPC:	High prevalence context
HSRC:	Human Sciences Research Council
ICER:	Incremental cost-effectiveness ratios
KZN:	KwaZulu-Natal
LM:	Limpopo
LPC:	Low prevalence context
MP:	Mpumalanga
MRC:	Medical Research Council
NACOSA:	National AIDS Convention of South Africa
NC:	Northern Cape
NV:	Nevirapine
NW:	North West
PMTCT:	Prevention of mother-to-child Transmission

QALYs: Quality-adjusted life years

SANAC: South African National AIDS Council

SE: Socio-economic

SPMS: Spectrum Policy Modelling System

STD: Sexually transmitted diseases

VCT: Voluntary counselling and testing

UNAIDS: Joint United Nations Programme on HIV/AIDS

WC: Western Cape

Chapter 1 : Introduction

Few studies have analysed claims that the different ways in which HIV/AIDS interventions interact with epidemiological and socio-economic contexts might result in different cost and effectiveness for such interventions (Hogan *et al.*, 2005; Verguet & Wash, 2010). In South Africa, in particular, where the impact of HIV/AIDS varies according to prevalence and socio-economic milieu (HSRC/MRC/CADRE, 2005; 2009) there have not been many CE comparisons of major HIV/AIDS interventions across these contexts except for studies comparing South Africa and other countries (Verguet & Wash, 2010, Dowdy *et al.*, 2006). The aim of this study is to compare the relative CE of several HIV/AIDS interventions in different epidemiological and socio-economic contexts in South Africa. This chapter outlines the background, problem statement, objectives, methods, and structure of the thesis.

1.1 Background and context of the study

The idea of comparing the relative CE of HIV/AIDS interventions in South Africa originated from my personal observation in 2010 that HIV-positive members of some households in Durban, South Africa, were not adhering to highly active antiretroviral (HAART) treatment because of stigma. They feared to be seen taking antiretroviral (ARV) pills. Today, stigma remains a concern in South Africa (DeKoker *et al.*, 2010; Pitpitan *et al.*, 2012).

My observation led me to believe that there would be different levels of health outcomes and costs across households with different levels of adherence rates to HAART given the evidence that non-adherence leads to virus resistance which in turn raises the cost of treatment (Bangsberg *et al.*, 2001). In the process of crystallising ideas by reviewing the literature, the fear of stigma on the part of HIV-positive patients in Durban households found explanation in social theories. According to these theories, social factors such as stigma affect health outcomes through their effect on individual behaviour and attitudes towards treatment and prevention interventions (Becker, 1974; Bandura, 1986; Glanz *et al.*, 1990; Fishbein & Ajzen, 1975; Fishbein *et al.*, 1991; Airhihenbuwa, 2004).

Such household-related social factors and the resulting impact of HIV/AIDS are likely to depend on the contexts of households, making these contexts important determinants of the effectiveness of HIV/AIDS interventions. Furthermore, HIV/AIDS interventions influence the impact of HIV/AIDS by directing specific activities to that impact. Because the impact of HIV/AIDS depends on the contexts, so, too, do the activities of HIV/AIDS interventions and therefore their costs.

These observations relating to the dependence of the costs and effectiveness of HIV/AIDS interventions on household contexts were extended from households to broader epidemiological and socio-economic contexts. By definition, a context is a circumstance with specific characteristics which differentiate it from another situation. In terms of this study, epidemiological contexts refer to two contexts, the low HIV prevalence context (LPC) or area, and the high HIV prevalence context (HPC) or area. Similarly, socio-economic contexts refer to two contexts, the rural context or area and the urban context or area. While context and area are considered synonymous in this study, the term context is preferred and is mainly used in this thesis.

Extending the dependence of the cost and effectiveness of HIV/AIDS interventions on household contexts to broader geographical contexts appeared to hold potential for greater efficiency in resource allocation. Because of the differences in the factors influencing the impact of HIV/AIDS in each context, differences in the effectiveness and costs of HIV/AIDS interventions were anticipated. The existence of lower (Western Cape, Northern Cape, Limpopo and Mpumalanga) and higher (KwaZulu-Natal, Gauteng, Free State, Eastern Cape and Northern Cape) HIV/AIDS prevalence provinces (Gouws, 2010:78) as well as the rural and urban contexts indicated that differences in the CE of HIV/AIDS interventions were possible.

An early scan of the literature revealed that there has been little research on the CE of HIV/AIDS interventions across epidemiological and socio-economic contexts in South Africa. All these factors led to the idea of estimating and comparing the CE of major HIV/AIDS interventions in epidemiological and socio-

economic contexts in South Africa, so as to assist policy makers in resource allocation in such contexts.

At the time of my observations, studies had shown the benefits of integrating HIV/AIDS interventions with primary health care such as tuberculosis (TB) care, treatment of sexually transmitted infections and reproductive health (Peck *et al.*, 2003; Church & Mayhew, 2009). Some evidence on the benefits of integrating HIV services with other primary health care services also existed in South Africa but focused mainly on the integration of HIV services with TB services (Coetzee *et al.*, 2004; Wallrauch *et al.*, 2010). At the start of this study, pilot projects for integrating HIV/AIDS services with primary health care were carried out in the UMgungundlovu Municipality in Pietermaritzburg to assess the benefits of integration with a view to implementing such integration on a large scale. The Municipality included a number of different epidemiological and socio-economic contexts.

The study expected to use cost and HIV/AIDS outcome data from these pilot projects as baseline information. The intention was to compare the CE of integrating primary health care with major HIV/AIDS interventions *versus* not integrating. Comparison of the relative CE of HIV/AIDS interventions in rural, urban, low, and high HIV prevalence contexts in South Africa was to be conducted by supplementing data from the pilot projects with other cost and effectiveness evidence.

Unfortunately, as is often the case in the South African public service, the early promise by municipal and provincial officials to facilitate access to the data did not materialise. Given my conviction of the importance of the study, I resolved to analyse the CE of HIV/AIDS interventions in different epidemiological and socio-economic contexts in the country, combining modelled data on costs and health outcomes and the evidence from the literature.

1.2 Impact of HIV/AIDS

Worldwide, the impact of HIV/AIDS has remained sufficiently significant to warrant a continued search for better options to respond to it. In 2011, about

33.2 million people were living with HIV/AIDS worldwide (Joint United Nations Programme on HIV/AIDS, [UNAIDS], 2011b). The worrying pattern of HIV infection has been its differentiated impact. Sub-Saharan Africa bears the brunt of the epidemic's burden, with 22.5 million of her population living with HIV/AIDS. Southern Africa has the highest HIV/AIDS prevalence on the African continent with countries such as South Africa, Botswana, Zimbabwe and Swaziland recording a prevalence rate of 15% to 30% (UNAIDS 2011 a). Women suffer the greatest burden of the epidemic, with 60% of all affected people worldwide being female, of whom 75% are in the age group 14-25 years (UNAIDS, 2011a).

South Africa has more people living with HIV/AIDS than any other country in the world, with the number of people living with HIV/AIDS estimated at over 5 million in 2013 (Statistics South Africa, 2013). Furthermore, the country has experienced rapid growth in new infections, increasing from 0.7% in 1990 to 12% in 1996. Since the mid-2000s, the number of new infections has stabilised and currently, it is expected to decline. However, new infections are still unacceptably high. In 2011, new infections for 2012 were projected at 110,000 (Actuarial Society of South Africa, 2011). While deaths from AIDS were alarmingly high in the late 1990s and early 2000s, amounting to hundreds of thousands per year, these cases have dropped significantly since 2007 due to the widespread rollout of antiretroviral drugs. Despite the decreasing death rates, the impact of HIV/AIDS remains significant, with about 100,000 AIDS-related deaths projected for 2012 in 2011 (Actuarial Society of South Africa, 2011).

As in other parts of the world, the HIV/AIDS epidemic in South Africa presents a differentiated impact. HIV/AIDS affects segments of the South African population to varying degrees. People with a low socio-economic status are hardest hit by the epidemic, females suffer the burden more than males, and young people aged 15-25 are the most affected, while the province of KwaZulu-Natal suffers the highest burden of the epidemic (Gouws, 2010). Given the link between HIV/AIDS health outcomes and other socio-economic woes, the differentiated impact of HIV/AIDS in terms of health outcomes implies differentiated impact in non-health outcomes. In fact, the health impact of HIV/AIDS leads to significant

socio-economic ramifications which are detrimental to current and future developmental prospects. The HIV/AIDS epidemic affects the survival of both households and firms and constitutes a barrier to human capital and economic development. Thus, the differentiated impact of HIV/AIDS requires a differentiated response.

1.3 HIV/AIDS interventions, effectiveness and challenges

HIV/AIDS interventions evolved over time and followed the changing response strategies. Prevention interventions progressed from the Department of Health's measures applicable to the usual infectious diseases (Zwi & Bachmayer, 1990:320), to more comprehensive measures involving many stakeholders beyond the Department (Department of Health, 2000). This evolution is marked by changes in the bodies that dealt with the response, each coming up with a strategic plan commensurate with the evolution of the epidemic to improve effectiveness. The bodies evolved from the Department of Health's AIDS Advisory Group in the 1980s (Zwi & Bachmayer, 1990:323), to the National AIDS Convention of South Africa (NACOSA) in the 1990s and the South African National AIDs Council (SANAC) in the 2000s (SANAC, 2012). Since 2000, SANAC's 5-year national strategic plans have been upgraded to tackle HIV/AIDS in a more effective and comprehensive manner (Department of Health, 2000; 2006; 2011).

While political irresponsibility deterred the effectiveness of HIV/AIDS interventions in the mid-2000s (Schneider & Stein, 2001, Fassin & Schneider, 2003; Johnson, 2004), the situation changed thereafter. Improved political and funding commitments after 2007 enhanced both prevention and treatment, and increased the number of people covered by both types of interventions. Furthermore, HIV/AIDS prevention interventions enhanced HIV/AIDS awareness and promoted changes in risky behaviours (Shisana & Simbayi, 2002; HSRC, 2005; 2009; 2013). The increasing rollout of ARV treatment reduced the number of AIDS cases and deaths (Walensky *et al.*, 2008). After 2007, the government adopted new guidelines that provided universal access to ARV services and more recently it adopted guidelines that allow for early access to antiretroviral

treatment (at CD4 count 350 rather than CD4 count 200)¹. This policy resulted in a more than 20-fold increase in the number of people accessing treatment; from 50,000 people in 2004 to more than a million in 2012 (Meyer-Rath, 2010). Increased access to treatment has translated into better health outcomes.

Despite the progress in responding to HIV/AIDS and the effectiveness of the interventions, South Africa still confronts a heavy HIV/AIDS burden. As the government strives to respond to the epidemic, an emerging challenge is the limited capacity and resources to implement such efforts. While recent efforts embraced the most effective strategies such as starting treatment earlier and offering HAART on a universal basis, the country faces resource challenges amidst current local and international economic turmoil (Walensky *et al.*, 2011: 27).

The problem is even more important in light of government's recent efforts to increase coverage of both prevention and treatment in the face of resource constraints. While it has been suggested that effectiveness can be improved at the same or lower costs by targeting interventions to some contexts (Grassly *et al.*, 2001), this has not been done in South Africa, where epidemiological contexts (an LPC and a HPC) and socio-economic contexts (a rural context and an urban context) present efficiency opportunities for such targeting. In particular the question of whether or not the CE of an HIV/AIDS intervention depends on the contexts, and if so to what extent, has not received sufficient attention in the literature on the CE of HIV/AIDS interventions in South Africa.

While recent literature in South Africa indicates that CE evidence can be used in different types of priority settings (Doherty, 2010), such evidence has not been sufficient to guide priority setting in different epidemiological and socio-economic contexts. The lack of contextual CE evidence may account for the limited contextual response in the country. Therefore, this study aims to contribute to this evidence.

¹ CD4 measures the strength of the immune system. The lower the CD4 count, the greater the impact of HIV/AIDS and the more an individual is vulnerable to HIV/AIDS.

1.4 Research objectives

The overall aim of the study is to compare the CE of a set of HIV/AIDS interventions in epidemiological and socio-economic contexts in South Africa. The specific objectives are:

- To provide an update on the nature, extent, trends and consequences of the HIV/AIDS epidemic in South Africa;
- To evaluate HIV/AIDS interventions and their CE in South Africa;
- To argue the case for the CE of HIV/AIDS interventions across HIV/AIDS epidemiological and socio-economic contexts in South Africa;
- To estimate and compare the CE of HIV/AIDS interventions in epidemiological and socio-economic contexts in South Africa; and
- To offer policy recommendations on how to conduct HIV/AIDS interventions in epidemiological and socio-economic contexts in the country in a cost-effective manner.

1.5 Research methodology

Comparing the CE of every modelled HIV/AIDS intervention across a rural context and an urban context or across an LPC and a HPC requires an estimation of the costs and effectiveness of that intervention in each of these contexts. Such estimation entails a follow-up of patients and a record of cost and effectiveness of that intervention. However, such follow-up is costly and provides cost and effectiveness estimates only up to the point of follow-up, while policy makers need such estimates beyond this point for planning purposes. In such a case, modelling is usually used to avoid the cost of a physical follow-up and to allow an estimation of future costs and effectiveness. To these end two approaches to modelling are used in this study.

The first approach uses Markov modelling. This modelling uses a hypothetical cohort of patients whose size changes over time only as a result of deaths. The model tracks a cohort of patients in each context over their lifetime since 2007. In other words, the model tracks patients in HIV/AIDS stages until almost all patients (95%) are dead. The year 2007 is chosen as a starting year to take into

account the time when the South African Government started to seriously commit to HIV/AIDS response. The estimation of the costs and effectiveness of HIV/AIDS interventions is expected to assess the costs and health benefits of such a commitment. The Markov Model tracks the cohort of patients over time by assuming the initial distribution of the patients in HIV stages based on the estimates from the literature on South Africa and the current evidence on the transition of patients from one HIV stage to another in South Africa.

The transition of patients in HIV/AIDS states over time in an LPC and a HPC are based on the projections of the AIDS model of the Actuarial Society of South Africa (ASSA) which depicts the dynamics of HIV/AIDS interventions in these contexts. Similarly, the transition of patients in HIV/AIDS states over time in a rural context and an urban context is assumed on the basis of the projection estimates of Spectrum Policy Modelling System (SPMS). The ASSA AIDS model projects population over time per province. Provinces making up either an LPC or a HPC are determined through an arbitrary antenatal HIV prevalence rate threshold of 25%. A province whose antenatal prevalence rates are below this threshold is designated an LPC and provinces whose prevalence is above the threshold are HPCs. Antenatal HIV prevalence in an LPC has been shown to be consistently lower than it has been in a HPC (Gouws, 2010).

Following the distribution of patients in HIV stages over time, the costs determined from the evidence in the literature are applied. The data on costs in this model are derived from CE evidence in South Africa from which the base-case values and their ranges are estimated. Health outcomes are measured based on patients' distribution in HIV/AIDS stages over time. The study applies utility weights (percentage of perfect health in a given HIV/AIDS state in a year) data from the South African literature to estimate the number of life-years free of ailment, the quality adjusted life years (QALYs) in each intervention. Utility weights are estimated by quality of life researchers and in the case of this study, were drawn and adapted from the main studies on health-related quality of life (O'Keefe *et al.*, 1996; Jelsma *et al.*, 2005; Louwagie *et al.*, 2007). Markov modelling estimates the total costs by summing up the costs in HIV/AIDS states over time. Similarly, the health outcomes are estimated by summing up the health outcomes in HIV stages over time.

The second modelling approach uses population projection models. These models project estimates of a changing size of patients over time due to deaths, migration and new births and compare estimates across contexts. The models used in this respect are the ASSA AIDS model and SPMS model. These models project the effectiveness of HIV/AIDS interventions in terms of infections and death averted and the number of patients using interventions based on the interventions' coverage rates. To produce cost-effectiveness estimates over time, particularly for the period 2007-2020, the study uses projected annual estimates of the number of patient-years using interventions from the ASSA AIDS and SPMS models. Annual costs per patient sourced from the South African and African literature are applied to the patient-years using interventions as projected by the models.

In this analysis, the CE comparisons across a rural and an urban context are limited to HIV/AIDS interventions modelled by SPMS, while the comparisons across an LPC and a HPC are limited to HIV/AIDS interventions modelled by the ASSA AIDS model. HIV/AIDS interventions modelled by the ASSA AIDS model are prevention of mother-to-child transmission (PMTCT), the treatment of sexually transmitted diseases (STD), voluntary counselling and testing (VCT) and highly active antiretrovirals (HAART), while interventions modelled by SPMS are HAART FOR ADULTS, HAART FOR CHILDREN and PMTCT.

The effectiveness of HIV/AIDS interventions in epidemiological contexts are compared on the basis of the infections averted for prevention interventions and deaths averted for treatment interventions. The costs are estimated based on the annual number of patient-years in each context and on the evidence of the annual estimates of costs per patient. The study uses the discount rate of 3% (Gold *et al.*, 1996) and measures the costs in US\$ dollars using the 2010 exchange rate to facilitate comparison with other studies. Sensitivity analysis is used on various uncertain parameters; details of this analysis are provided in specific chapters. The CE of an HIV/AIDS intervention is compared across an LPC and a HPC or across a rural and an urban context. In this analysis, an intervention is considered more cost-effective in context one than in context two

when the cost per health outcome in context one is lower than that of context two.

1.6 Structure of the thesis

This thesis is organised into ten chapters to achieve the study's objectives. Each chapter addresses a specific aspect of the study.

Chapter one introduces the subject matter of the study. It provides the background, purpose, problem statement, objectives of the study, overview of the methodology and structure of the thesis.

Chapter two provides an update on the impact of HIV/AIDS in South Africa. It highlights the nature of the impact of HIV/AIDS, explores HIV/AIDS impact studies, and examines the trends and extent of the impact of HIV/AIDS by means of the best AIDS models in South Africa.

Chapter three examines the extent to which HIV/AIDS interventions have been conducted in South Africa. More precisely, it elaborates on the extent to which HIV/AIDS interventions have been targeted.

Chapter four presents the CE evidence of HIV/AIDS interventions in South Africa with a view to justifying the need for such studies. It also scrutinises the evidence on the basis of the studies' patterns, the extent to which they have covered important HIV/AIDS policy aspects and particularly the extent to which they have compared CE interventions across rural/urban and low/high prevalence contexts.

Chapter five argues the case for CE comparisons of HIV/AIDS interventions in different contexts. It focuses on the case for the CE comparison of HIV/AIDS interventions across epidemiological and socio-economic contexts.

Chapter six explains the general methodology used to compare HIV/AIDS interventions across contexts. It describes the modelling approach used, the process of data collection and the manner in which uncertainty is handled.

Chapter seven compares the CE of intervening in an LPC and a HPC in South Africa. The comparison is carried out with Markov states transition models.

Chapter eight compares the CE of HIV/AIDS interventions across a rural context and an urban context. It also uses the Markov states transition models.

Chapter nine compares the CE of HIV/AIDS interventions in epidemiological and socio-economic contexts. In this case, projection models are used to conduct the analysis from a different point of view.

Chapter ten provides the summary, conclusions and policy recommendations. The summary recapitulates the main aspects of the research process. The conclusions highlight the main findings, while the recommendations offer policy proposals and suggestions for further research.

Chapter 2 : Socio-economic and epidemiological impact of HIV/AIDS in South Africa: An update

This chapter provides an update on the socio-economic and epidemiological impact of HIV/AIDS in South Africa. Following a discussion of the nature of the impact of HIV/AIDS in section one, an overview of HIV/AIDS impact studies is presented in section two. Section three presents the extent of the impact; and section four discusses the trends; while section five examines the distribution patterns of the impact.

2.1 Nature of the impact of HIV/AIDS

The impact of HIV/AIDS consists of a direct effect on the health status of the infected and an indirect effect on the society in which the infected person lives. The impact of HIV/AIDS begins with the acquisition of the HIV virus *via* blood contact through needle sharing or injury, unprotected sexual intercourse, during pregnancy, at birth or during breastfeeding. Once the HIV virus enters the body, it replicates and progressively destroys the body's protective system. This eventually weakens the system and makes it vulnerable to diseases which at some point become serious (AIDS) and ultimately lead to the death of the infected person.

While the impact of HIV/AIDS is first observed at an individual level, it has far reaching ramifications. HIV/AIDS primarily affects the most economically active population between 24 and 59 years old who in most cases are also heads of households (Booyesen *et al.*, 2004). By killing heads of households or causing their disability, HIV/AIDS not only imposes current impact but also attracts future socio-economic consequences for households and society at large.

At the household level, the socio-economic impact of HIV/AIDS commences with the partial loss of income as a result of illness, estimated to be higher in affected households than non-affected ones (Bachmann & Booyesen, 2003). HIV/AIDS leads to the total loss of income when the infected person dies (Casale & Whiteside, 2006; Naidu & Harris, 2006). In most cases, HIV/AIDS changes

households' patterns of expenditure from investment (in education, for example) towards consumption. This pattern ultimately results in poverty. The mechanism through which HIV/AIDS impoverishes households is the simultaneous loss of income and the erosion of accumulated wealth as household members are obliged to draw on savings (Freire, 2004; Collins & Leibbrandt, 2007), other wealth and borrowings to provide treatment for the infected persons, to pay for their funerals or to cover other basic household needs. While some studies on the impact of HIV/AIDS have focused on the mechanism through which AIDS induces poverty, others note that the relationship is simultaneous (Tladi, 2006). Infected families' unwillingness to save/invest in the future because of their focus on present realities has also been identified as a mechanism through which HIV/AIDS induces poverty (Booyesen *et al.*, 2004).

Furthermore, studies have found that in most cases, these effects spread to the infected person's community and to the broader society in the form of support from extended families and social assistance from government and non-governmental organisations. At community level, the socio-economic burden of HIV/AIDS extends to relatives of the infected in the form of care provided by extended family members for the infected person or their children during sickness and after death. In many cases, this consists of sending members of extended families to affected households or taking the infected or their children into non-affected or least affected extended families. A study by Raniga & Simpson (2011) found that, in KwaZulu-Natal, some households which received old age state pension were more impoverished due to caring for grandchildren infected with HIV/AIDS.

At societal level, the socio-economic impact is also diverse and includes an increase in morbidity, mortality and excessive demands on the public health system (Zelinick & O'Donnell, 2005). Illness and death among public servants lead to a shortage of essential services such as education and health care, and there is a reduction in productivity and economic growth (Arndt & Lewis, 2001), an increase in social assistance spending and reduced human capital accumulation.

2.2 Overview of HIV/AIDS impact studies in South Africa

The impact of HIV/AIDS in South Africa has been studied extensively. These studies can be categorised based on the scope of analysis: micro-level (households, firms, individuals) or macro-level (regional or nationwide) studies. Furthermore, the studies can be categorised on the basis of the direct health impact (new infections, morbidity and mortality) or the indirect health impact (socio-economic and demographic consequences). A summary of representative studies is provided in Table 2:1.

Table 2:1 Summary of representative studies of the impact of HIV/AIDS in South Africa

Parameter	Study characteristics	General description	Examples
The level of study	Micro studies	These studies compared affected households in which one member was infected and non-affected households in the neighbourhood comparing a set of variables ranging from expenditure to financial response, quality of life, and short and long-term income.	(Bachmann & Booysen, 2003; Bachmann & Booysen, 2004; Booysen <i>et al.</i> , 2004, O'Keefe & Wood, 1996, Collins & Leibbrandt, 2007).
	Macro studies	Analysed the impact on factors such as economic growth and unemployment using models that project over time, based on the effect of HIV/AIDS on different sectors of the economy and the link between supply and demand of factors of production over time.	(Bollinger & Stover, 1999; Booysen <i>et al.</i> , 2003; Arndt & Lewis, 2001; Connolly <i>et al.</i> , 2004, Vass, 2007).
Types of impact	Direct health impact	These studies analysed the impact of HIV/AIDS on morbidity whether at household, sector or macro levels, reporting morbidity, mortality, life expectancy etc.	(Bachmann & Booysen, 2003; Johnson & Dorrington, 2006; Rehle & Shisana, 2003).
	Indirect socio- economic impact	These studies reported the consequences in terms of poverty, social problems, patterns of spending, skills, etc.	(HSRC/MRC/CADRE, 2009).

Source: Compiled from the literature by the author

Table 2:1 indicates that micro-impact studies compared the impact at the household and firm levels and typically compared affected with non-affected households or firms. Affected households were in most cases identified *via* HIV service providers and unaffected households in the vicinities of affected households were used as controls (Bachmann & Booysen, 2003; Naidu & Harris, 2006). These studies assessed the impact of HIV/AIDS by comparing patterns of spending, health status, use of health care services, and borrowing.

Macro-impact studies used population and epidemiological projection models to estimate and simulate the impact on morbidity and mortality which in turn was used to estimate the loss in productivity and other socio-economic consequences. They measured the impact by comparing estimates of economic growth, unemployment, life expectancy and mortality in the absence and presence of HIV/AIDS or in the absence or presence of interventions (Johnson & Dorrington, 2006). Some studies simulated the impact to take the interactions between different sectors of the economy into account and used computable general equilibrium models. Arndt & Lewis's (2001) study is the most recent of these kinds of studies.

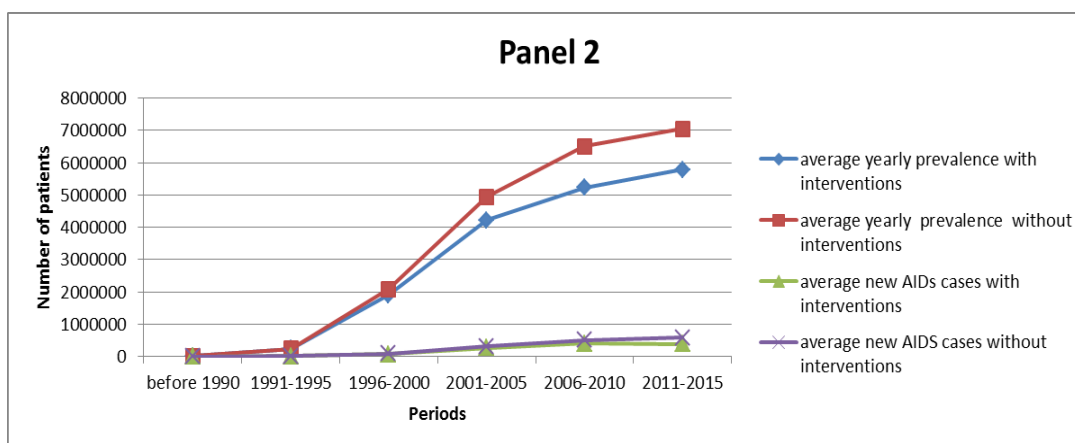
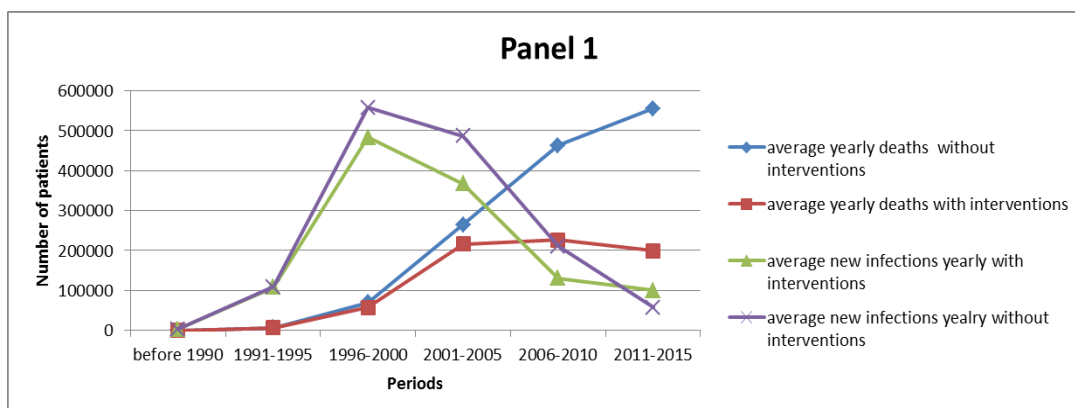
In terms of the type of impact measured, some studies assessed the direct impact of HIV/AIDS on health status, whilst others studied the indirect consequences. The studies that measured the direct health impact reported the impact of HIV/AIDS on mortality and morbidity (Johnson & Dorrington, 2006). Those that examined indirect effects reported the impact of HIV/AIDS on education, orphanhood, economic growth, and unemployment (Johnson & Dorrington, 2006).

Since most of the studies that documented the impact of HIV/AIDS date back to 2007 or earlier, there is a need for an update. Given that time, space and data availability do not allow for an update on the non-health impact of HIV/AIDS on households, changes in macro HIV/AIDS health variables such as new infections, AIDS cases and deaths can assist in making inferences about the impact of HIV/AIDS on socio-economic variables and micro entities. The discussion which

follows relies mainly on the projections of the ASSA AIDS model to provide an update on the extent, trends and patterns of HIV/AIDS in South Africa. The discussion begins with the extent of the impact of HIV/AIDS.

2.3 Extent of the impact of HIV/AIDS in South Africa

HIV/AIDS has thus far killed three million people in South Africa and currently 5.5 million people are living with the disease (Statistics South Africa, 2011). While HIV/AIDS's impact has been devastating in the past, the extent of its impact in more recent times is not well reported, except for anecdotal reports that the impact has decreased. In this section, the ASSA AIDS model is used to provide an update on the extent of the impact of HIV/AIDS in terms of new infections, prevalence, AIDS, and deaths. The data are presented in Figure 2:1.



Source:

Results extracted from the ASSA (2011)'s full AIDS and Demographic model of the Actuarial Society of South Africa as downloaded (10/01/2012) from www.assa.co.za.

Figure 2:1 Change in new infections, death cases, prevalence and AIDS cases over time in South Africa

Panel 1 of Figure 2:1 shows that the number of new infections in South Africa was insignificant in the period before 1990. However it increased rapidly in subsequent periods, reaching a peak in the period 1996-2000 before starting to decrease. The number of new infections increased from an annual average of 3,000 new infections in the period before 1990 to 100,000 new infections in the period 1991-1995 and to an average of 480,000 new infections in the period 1996-2000. The number of new infections decreased thereafter to 360,000 in the period 2001-2005 and to an average of 130,000 new infections in the period 2006-2010. According to projections, new infections are expected to continue decreasing to less than 100,000 new infections per year over the period 2011-2015.

There were very few AIDS deaths before 1995. Thereafter, the country started experiencing an increase in these deaths. In the period 1996-2000, AIDS deaths reached an annual average of 50,000. From 2001 to 2005, AIDS deaths increased to 210,000 per year, the highest since the advent of HIV/AIDS in South Africa. However, the number of deaths remained high over the next period (2006-2010). The number of annual AIDS deaths is projected to decrease slightly to 200,000 for the period 2011-2015.

Analysing the impact in terms of people living with HIV/AIDS in the same period, Figure 2:1, Panel 2 indicates an insignificant number of people living with HIV before 1990. In the period 1991-1995, however, the average number of people living with HIV/AIDS increased to about 20,000. In the period 1996-2000, the number was about 200,000; from 2001-2005 it was around 420,000; and from 2006-2010 it was about 520,000; while it is estimated at 560,000 for 2011 - 2015. This continued increase in the number of people living with HIV/AIDS is expected because of the persistence of new infections, although at a decreasing rate. The increase in prevalence can also be explained on the one hand, by the widespread impact of HAART, which prolongs the lives of people living with HIV/AIDS, while on the other, it might reflect an increase in the natural survival of HIV/AIDS patients. While survival is a good thing, it comes at the cost of increased health care.

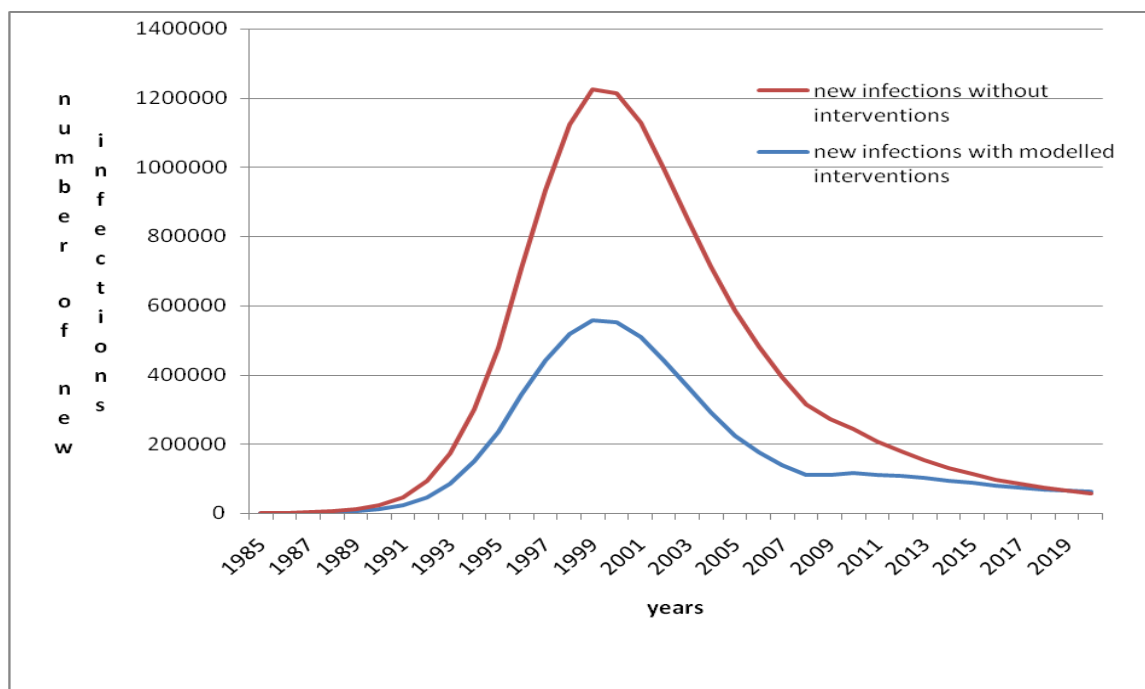
It is worth noting, however, that the impact of HIV/AIDS has been significantly affected by the success of HIV/AIDS interventions, particularly HAART in terms of survival. This is observed in Figure 2:1 (both panels), which compares scenarios of absence of HIV/AIDS interventions with scenarios where such interventions are present.

In the absence of HIV/AIDS interventions, additional new infections in the period 2006-2010 would have been about 100,000; and additional new deaths would have been 250,000, while 250,000 additional people would have been living with HIV/AIDS. HAART in particular has reduced mortality; in 2009, 52% of all deaths in the country were related to HIV/AIDS whilst in 2012 only 43.6% were related to

HIV/AIDS and life expectancy increased from 54 to 60 years (Abdool Karim, 2012). Figure 2:1 Panel 1 shows that even in the absence of HIV/AIDS interventions, the number of new HIV infections and AIDS deaths would eventually decrease after a long period. This evidence reflects the fact that the reduction in new infections could take place naturally over time, whilst people also tend to resist HIV/AIDS-related deaths as time progresses.

2.4 Trends in the impact of HIV/AIDS

Analysed from the point of view of new infections, three periods mark the trends in the number of new infections. These periods consist of a period of almost no impact (1980-1990); the period of exponential increase in the impact (1991-1999) and the period of decrease in the impact (2000 onwards). Figure 2:2 shows these data.

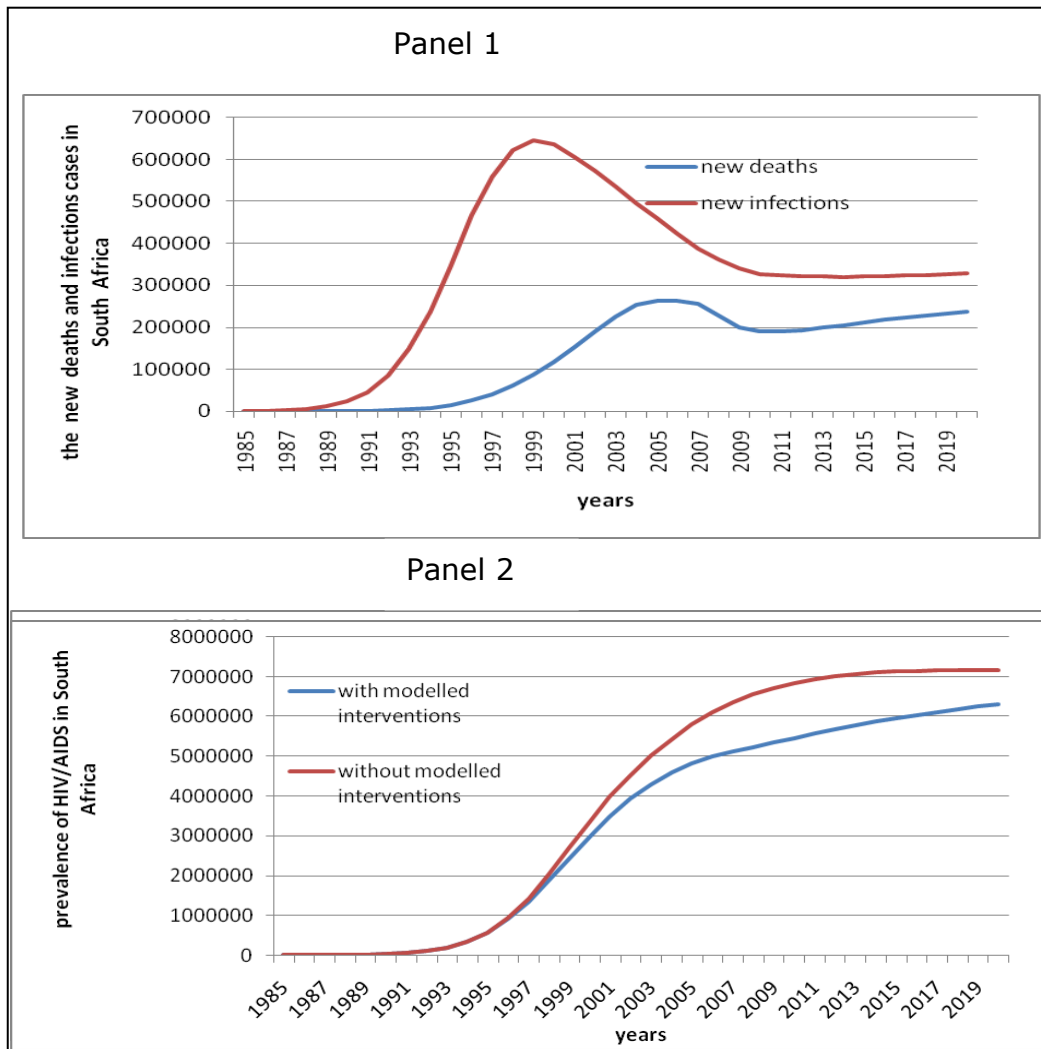


Source: Results extracted from the ASSA (2011) full AIDS and Demographic model of the Actuarial Society of South Africa as downloaded (10/01/2012) from www.assa.co.za.

Figure 2:2 Trends in new cases of infections in South Africa

As Figure 2:2 shows, in the first ten years (1980-1990) after the outbreak of HIV in South Africa, less than 1,000 new infections were reported annually. However, the number of new infections increased exponentially from 1,000 in 1991 to about 580,000 in 2000. Since 2000, there has been a decrease in new infections which can be partly explained by the impact of HIV/AIDS interventions and partly by the natural evolution of the epidemic. The natural evolution of the epidemic is depicted by the curve representing the projection of the number of new infections in the absence of HIV/AIDS interventions. This curve shows that the decrease in the number of new infections would have started after 2000 even in the absence of interventions (Figure 2:2). From 2000 to 2012, the number of new infections was projected to decrease from 580,000 to 80,000.

The trend in the number of people living with HIV/AIDS (prevalence) is expected to follow the trend in the number of new infections since prevalence, the total number of people infected with HIV/AIDS at a given point in time, is the cumulative number of new infections before that time. However, prevalence can be affected by the number of deaths. In the case of South Africa, the number of new infections has been always higher than the number of deaths and is projected to remain higher at least until 2015. Figure 2:3 shows the results.



Source: Results extracted from the ASSA (2011) full AIDS and Demographic model of the Actuarial Society of South Africa downloaded (10/01/2012) from www.assa.co.za

Figure 2:3 New deaths and infections and prevalence in South Africa

The higher number of new HIV infections relative to AIDS deaths over time shown in Panel 1 of Figure 2.3, explains why prevalence has been increasing. The period with the highest number of deaths, 1997-2005, coincided with an ever-increasing number of new infections, except for 2000-2005, when the number of new infections started decreasing, but remained significantly greater than the number of deaths (See Figure 2:3 Panel 1). Because the number of new infections has been significantly higher than the number of deaths, the trend in prevalence has followed the trend in the number of new infections. Prevalence increased sharply in the

period 1993-2003 from 200,000 people living with HIV/AIDS in 1993 to about 5 million people living with HIV/AIDS in 2003.

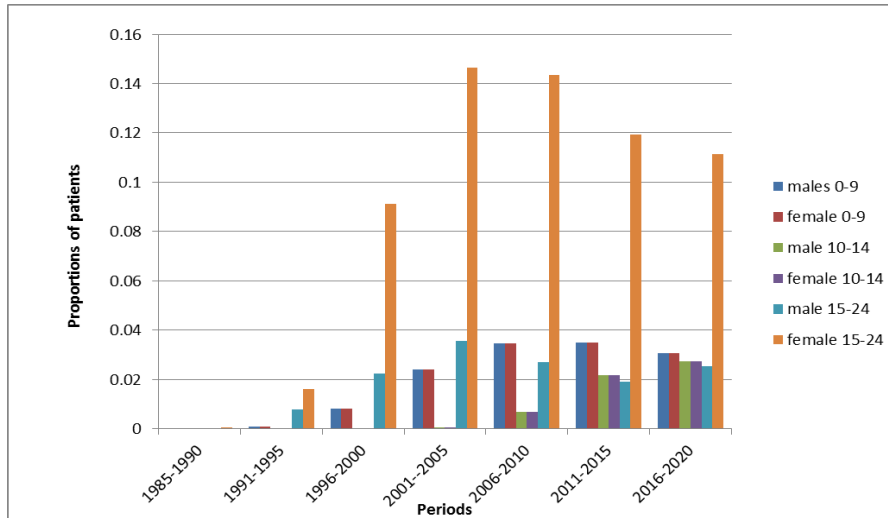
Likewise, three periods can be distinguished when analysing the trend of the impact in terms of deaths. Figure 2:3 Panel 1 shows that in the period 1980-1993, the number of AIDS deaths was almost zero. During 1995-2005, the number of deaths increased from 20,000 to 280,000, while from 2005, the number of AIDS deaths started decreasing. In 2011, the number of AIDS deaths stabilised at 200,000 although the projections suggest a slight increase in the future. Since the time of death is very close to the time of onset of AIDS, especially in the absence of intervention (on average, death takes place one year after the onset of AIDS), these statistics indicate that suffering caused by AIDS is still significant in South Africa. Figure 2:3 Panel 2 shows that, prevalence, and thus new infections would have been higher in the absence of HIV/AIDS interventions.

2.5 Distribution Patterns of the impact

HIV/AIDS has affected different segments of the South African population, and epidemiological and socio-economic contexts to a different extent. The literature notes that HIV/AIDS has a greater impact on women; younger people aged 15-25, in a rural context, and in some provinces (Gouws, 2010). This section provides an update on the impacts to ascertain whether these patterns have persisted or changed.

2.5.1 Gender and age

HIV/AIDS has affected men and women to a different extent in South Africa. The data from the ASSA AIDS model in Figure 2:4 show these differences.



Source: ASSA (2011). Note prevalence rate as percentage of total population and not as percentage of susceptible population because of lack of data

Figure 2:4 Changes in proportions of people living with HIV/AIDS in the presence of HIV/AIDS interventions

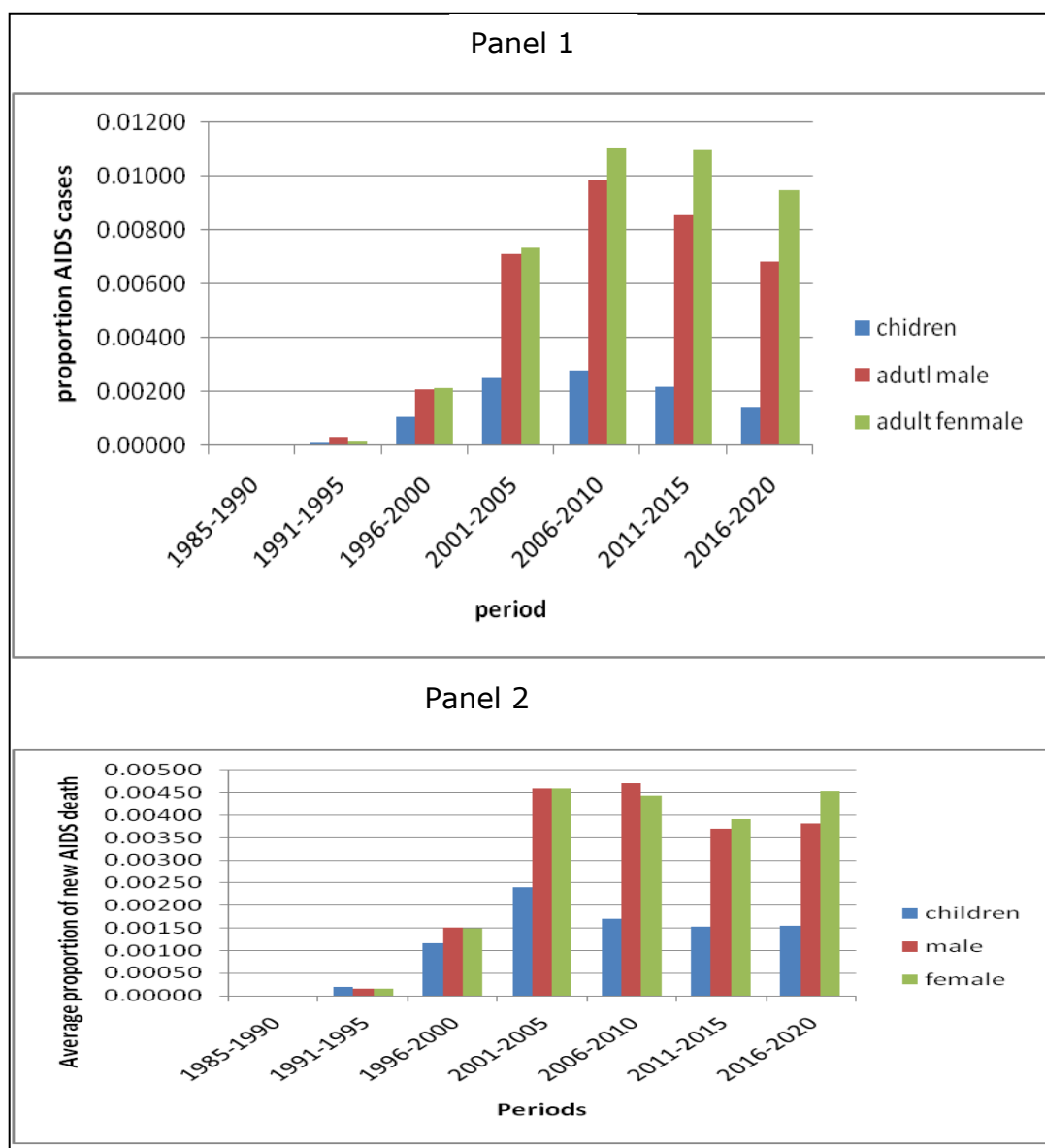
Figure 2:4 shows that, females aged 15-24 years have been the most affected. The prevalence rate of females in this age group increased from 2% in the period 1991-1995, to 15% in the period 2001-2005 and 14% in the period 2011-2015. The respective prevalence rates among males in the same age group are 1%, 5% and 3%. The data suggest that the patterns in the impact of HIV/AIDS in this age group have not changed (ASSA, 2011).

However, the prevalence patterns have changed in younger people in the age groups 0-9 and 10-14 years. Figure 2:4 shows that in the period before 1995, HIV was not prevalent among these age groups. However, from 1996-2000, the proportion of children aged 0-9 living with HIV/AIDS reached around 1%. In the period 2006-2010, this increased to 3.5%. This proportion is projected to remain at this level in the period 2011-2015, although it is predicted to decrease thereafter. The data indicate that males and females in this age group, who may have acquired HIV mainly from their mothers, were equally affected (ASSA, 2011).

While HIV/AIDS was expected to be absent in the age group 10-14 years, given the assumption of the absence of sexual activity in this age group, it was surprising to

find that in the period 2006-2010, about 1% of children in this age group were living with HIV/AIDS (Figure 2:4). For the period 2011-2015, the proportion is projected at 2% with no difference in terms of gender, although it is projected to decrease in the future. Recent changes in the patterns of HIV/AIDS prevalence signify changes in risky sexual behaviours, with young people in South Africa engaging in sexual activities earlier than had been previously reported. Alternatively, this could be a result of antiretroviral therapy which is reported to prolong the lives of children infected by their mother from childhood to teenage and adulthood (World Health Organisation (WHO), 2007).

With regard to prevalence across age and gender, it would have been preferable to analyse the patterns of the impact of HIV/AIDS in terms of deaths across age groups and gender. However, detailed data for this analysis were not available. Therefore, the patterns of AIDS and cases of death across gender are analysed by examining the impact across adult males and females, and the impact across age is analysed by comparing the impact across children (less than 15 years old) and adults. Figure 2:5 provides these data.



Source: Results extracted from the ASSA (2011) full AIDS and Demographic model of the Actuarial Society of South Africa downloaded (10/01/2012) from www.assa.co.za

Figure 2:5 Composition of AIDS cases

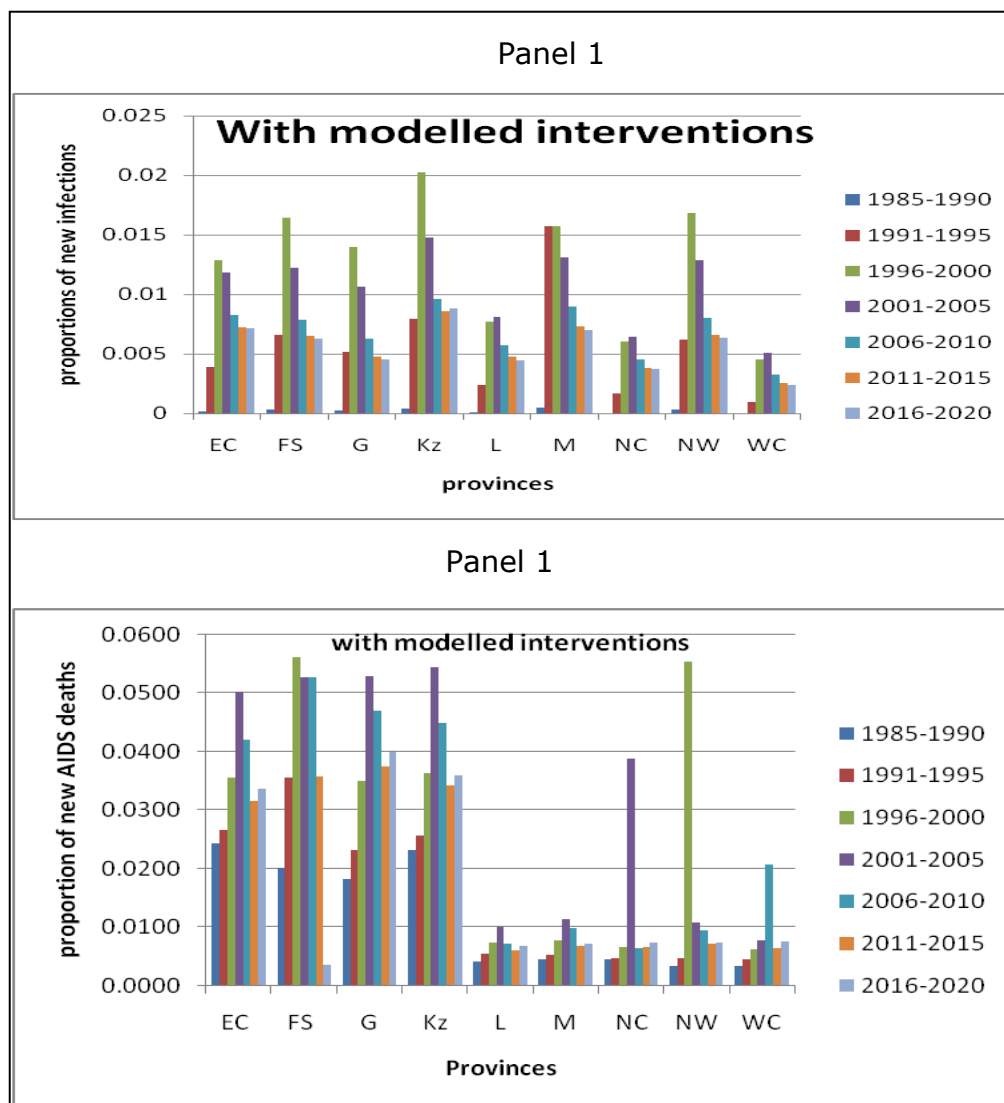
The data in Figure 2:5 show that the proportion of AIDS cases has been consistently higher among females than males, with the gap in the proportion of AIDS cases across gender increasing over time. Panel 1 of Figure 2:5 shows that the proportion of AIDS cases was the same across the genders in 1996-2000, about 20 cases in a population of 10,000 people. In 2001-2005, the number of AIDS cases started to differ. There were 70 AIDS cases for males in a population of

10,000 people, while the corresponding estimate for females was 72. In the period 2006-2010, there were 88 and 110 AIDS cases, respectively in a population of 10,000 people. For the period 2011-2015, the projected figures are 82 and 110. AIDS cases are projected to decrease but with increasing gaps across gender (ASSA, 2011).

AIDS death patterns across gender appear to generally follow the patterns of AIDS cases. Panel 2 of Figure 2:5 suggests that the number of AIDS deaths were similar across the genders in the periods 1991-1995, 1996-2000 and 2001-2005 with the number of deaths in a population of 10,000 people being 2.5, 15, and 45, respectively. AIDS deaths were higher among males (45 male deaths *versus* 42 female deaths) in a population of 10,000 in the period 2006-2010, while for the period 2011-2015, the number of AIDS deaths in a population of 10,000 is projected to be higher among females than males (38 female deaths *versus* 35 male deaths). The data indicate that the gap in AIDS deaths across gender is predicted to increase, with more females dying (ASSA, 2011).

2.5.2 Provincial impact

The impact of HIV/AIDS in terms of new infections and AIDS deaths has also been differentiated across South Africa's nine provinces. Panel 1 of Figure 2:6 shows, that some provinces have higher levels of infections than others.



Source: Results extracted from the ASSA (2011) full AIDS and Demographic model of the Actuarial Society of South Africa downloaded (10/01/2012) from www.assa.co.za

Figure 2:6 Impact of HIV/AIDS across provinces

The data in Panel 1 of Figure 2:6 indicate that in the period 1985-1990, the number of new infections was still insignificant but differences already existed across provinces. The top five provinces in terms of the proportion of infected people, with no clear ranking on the basis of the available information were: the Free State (FS), Gauteng (G), KwaZulu-Natal (KZN), Mpumalanga (M) and North West (NW). In the period 1991-1995, however, the statistics suggest some ranking. The top five, listed in descending order in terms of the proportions of the population infected,

were: KZN, FS, NW, G, and the Eastern Cape (EC). In the period 1996-2000, the top five were: KZN, FS, NW, M, and EC.

This ranking persisted in the following periods, suggesting that the burden of HIV infections has been disproportionately distributed across provinces with a specific set of provinces consistently emerging as the most affected over time. Not surprisingly, Panel 2 of Figure 2:6 show that, over time, these provinces have borne most of the burden of the HIV/AIDS epidemic in terms of deaths (ASSA, 2011).

2.5.3 Urban and rural impact

Finally, the differentiated impact of HIV/AIDS has been observed across rural and urban contexts. Although detailed differences in HIV infections, AIDS cases and deaths have not been modelled in urban and rural contexts in South Africa, the differentiated impact of HIV/AIDS across the two contexts has been documented. HIV/AIDS surveys in South Africa revealed that people in rural contexts were less aware of HIV/AIDS; knew less about how to avoid it; and practiced more risky sexual behaviours than their urban counterparts (Department of Health, 2003 c: 88). National HIV/AIDS prevalence surveys showed that prevalence was higher in a rural context than in an urban context (Shisana & Simbayi, 2002). Furthermore, micro studies indicated that greater poverty in a rural context interacted with HIV/AIDS to yield worse HIV/AIDS outcomes (Bachman & Booysen, 2003).

Chapter summary

This chapter provided an overview of the impact of HIV/AIDS in South Africa with respect to the extent, trends and patterns of the impact of HIV/AIDS in terms of new HIV infections, AIDS cases and deaths. It revealed that although the impact is decreasing, it remains highly significant and is differentiated across age, gender, provinces and rural and urban areas. An increase in risky sexual behaviours among young people aged as young as 10-14 was noted as a new pattern of the epidemic. The next chapter examines the conduct of HIV/AIDS interventions in South Africa.

Chapter 3 : Analysis of HIV/AIDS interventions in South Africa

This chapter examines the extent to which policies to improve the effectiveness of HIV/AIDS interventions accommodated context-specific responses. The chapter starts with an overview of the conduct of HIV/AIDS interventions in section one. Section two discusses the effectiveness of HIV/AIDS interventions in South Africa. Section three examines the extent to which policies to improve the effectiveness of HIV/AIDS interventions have been implemented, while section four focuses on the extent to which these policies were context-specific.

3.1 Overview of HIV/AIDS interventions in South Africa

The conduct of HIV/AIDS interventions in South Africa has been very influenced by political leadership. In this overview, the conduct of HIV/AIDS interventions as well as the role of political leadership is emphasized.

3.1.1 Conduct of HIV/AIDS interventions

HIV/AIDS interventions in South Africa are a result of policy strategies which evolved over time. In South Africa, HIV/AIDS was initially dealt with like any other infectious disease by the Department of Health. The department's strategies included putting HIV patients in quarantine and only allowing immigrants who were HIV negative into South Africa (Zwi & Bachmayer, 1990). However, from the late 1980s and early 1990s, proper strategies to deal with HIV/AIDS were placed on South Africa's national agenda. The common feature of these strategies was that they took the multi-facet nature of the epidemic into account. This implied that the response was not limited to the activities of the Department of Health but to the concerted efforts of many stakeholders, both government and civil society. The strategies were refined over time through successive strategic five-year plans, 2000-2005, 2007-2011 and 2012-2016 (Department of Health, 2000; 2006; Department of Health /South African National AIDS Council, 2011).

The first official body to deal with HIV/AIDS in the country was the National AIDS Convention of South Africa (NACOSA) which was instituted in 1992 and chaired by non-politicians. The influence of political leadership in the response started with the involvement of a high level political body, the inter-ministerial committee in 1998, which was chaired by the then president of South Africa. In 2000, the inter-ministerial committee was replaced by the South Africa National AIDS Council (SANAC), also chaired by a politician, the Deputy President of the country (Department of Health, 2006).

A number of HIV/AIDS interventions emerged from the national strategic plans and political involvement in the HIV/AIDS response. Table 3:1 summarises these interventions per category.

Table 3:1 Categorisation of HIV/AIDS interventions in South Africa

target	Prevention interventions		Treatment and care interventions	
	Behavioural	Biomedical	Biomedical	Non-biomedical
Individual	VCT: provided at over 4000 testing centres countrywide (Walensky <i>et al.</i> , 2011)	PMTCT: Started in 2000 and is provided at different antenatal clinics throughout the country (Department of Health, 2000) Voluntary circumcision: Conducted at the request of clients VCT Treatment of STD	-HAART: Started officially in 2003 and is provided at dedicated clinics (Department of Health, 2003a) -Caring for TB and HIV and other infections -Caring For TB/AIDS co-infection (trial) 2007 (Abdool Karim <i>et al.</i> , 2009)	Individual psychosocial counselling
Group	Toll free line to provide AIDS information in 1991 Mass media -Pre-schoolers: Takalami sesame in 2000 (CADRE,2001) -Youth: TshaTsha in 2003 Kincaid & Coleman (2006) -HIV positive: (Gazlam) -Stigma: Phamokate -High school learners: peer groups -Primary school learners: peer groups -General public: Khomanani, Love life and Soul City mass media campaigns started in 1999 (Tufte, 2002, Parker, 2003) HIV/AIDS and Tuberculosis programme			Group psychosocial counselling

Source: author based on the reviewed literature on HIV/AIDS interventions. For some interventions, no specific starting date was found in the literature.

Table 3:1 shows that HIV/AIDS interventions can be placed in two main categories: prevention interventions and treatment interventions. Prevention interventions consist of interventions aimed at reducing the number of new infections while treatment interventions seek primarily to reducing suffering and death.

Prevention interventions can be categorised into behavioural interventions and biomedical interventions. Behavioural interventions consist of activities that seek to reduce infections through education about avoidance of risky behaviours. Biomedical interventions seek to reduce the occurrence of new infections by using biomedical practices.

Treatment and care interventions can be categorised into biomedical interventions and psychosocial counselling. Biomedical treatment interventions consists of interventions seeking to reduce suffering among the infected by means of medical or clinical care. Psychosocial interventions consist of interventions aiming to decrease suffering through trauma counselling.

In terms of the type of audience targeted by HIV/AIDS interventions, some interventions target individuals while others target groups of individuals. Most of the interventions targeting individuals are biomedical interventions. Biomedical prevention interventions offered at an individual level consists of PMTCT, pre-exposure prophylaxis, voluntary circumcision and treatment of sexually transmitted infections. In South Africa, prevention of mother-to-child HIV transmission started in 2000. PMTCT services have since expanded to the extent that they are provided in almost 95% of all public health care facilities countrywide (Goga *et al.*, 2010:x). Recently about 91% of all pregnant women who are HIV positive have been receiving antiretroviral prophylaxis and the rate of transmission decreased from about 15% in 2009 to 3.5% in 2011(Leach-Lemens, 2011). In 2009, SANAC put an accelerated plan in place to implement PMTCT in order to strengthen the supply and demand side of the programme (Department of Health, 2010 c). In contrast, the treatment of sexually transmitted diseases (STDs) among HIV/AIDS patients has not been given special attention in South Africa. However, treatment of STDs as a

strategy to reduce the risk of HIV transmission has been considered an important intervention both in South Africa (Johnson & Budlender, 2002; Johnson, 2008) and elsewhere (Sweat *et al.*, 2000; Price *et al.*, 2006). HAART started in 2003 and increased over time. In 2012, about 2 million people were on HAART across all 2,552 approved facilities in the country (IRIN/Plus News, 2012). While other interventions have been conducted as fully fledged responses to the impact of HIV/AIDS, Microbicide (Abdool Karim *et al.*, 2010), antiretroviral prophylaxis (Christofides *et al.*, 2006; Pretorius *et al.*, 2010) and voluntary circumcision (Kahn *et al.*, 2006) have been mainly conducted in the form of trials thus far.

Biomedical treatment interventions offered at individual level are HAART and treatment of TB and other opportunistic infections among HIV/AIDS patients. Another type of intervention offered at individual level is trauma counselling. Counselling is provided to patients to help them manage the shock experienced when they discover that they are HIV positive. Trauma counselling offers advice to patients on their behaviour and lifestyle and encourages them to adopt a positive attitude towards life while living with HIV/AIDS.

While most biomedical interventions have been offered at individual level, the opposite is true for behavioural interventions which were educational interventions delivered to groups of patients. These interventions consisted mainly of use of mass media in the form of HIV/AIDS-related drama, targeting different groups of people at risk. These drama programmes included *TshaTsha* in 2003, which targeted the youth (Kincaid & Coleman, 2006); *Gazlam* in 2003, which targeted HIV positive people; *Phamokate* in 2002, which targeted people with stigma and *Takalami Sesame* in 2000, which targeted pre-schoolers (CADRE, 2001). Concurrently, mass education using multimedia social campaigns such as Soul City which started in 1994 (Tufte, 2002: 2), Love Life which started in 1999 (Parker, 2003:1) and Khomanani which started in 2002 (National HIV/AIDS & Tuberculosis Programme, 2003) were implemented to modify individual and environment-induced HIV/AIDS risk behaviours. Educational interventions evolved further to target the reduction of

circumstances which facilitate risky behaviours such as poverty and violence against women even though they are still in their trial stages (Pronyk *et al.*, 2008).

Testing and counselling are interventions with educational and biomedical aspects. This HIV/AIDS intervention started in 2000, primarily to provide education at an individual level on how to avoid HIV infection, and secondarily to link infected patients to treatment. Testing and counselling services have expanded; there are currently more than 4,000 voluntary counselling and testing (VCT) centres in South Africa. In 2011, Walensky *et al.*, (2011: 26) reported that VCT was offered at 96% of public health care facilities.

3.1.2 HIV/AIDS interventions and political leadership

Although a fair number of HIV/AIDS interventions have been put in place, South Africa's political leadership failed to act on time (Chigwedere *et al.*, 2008). The literature on the politics of HIV/AIDS in South Africa (Schneider & Stein, 2001; Fassin & Schneider, 2003; Johnson, 2004) indicates that both the apartheid and post-apartheid governments failed to act at relevant times to reduce the impact of HIV/AIDS. The apartheid regime failed to put proper HIV/AIDS policies in place when HIV was nascent, while the post-apartheid leadership, despite having proper HIV/AIDS policies in place, was plagued by competing political priorities and misinformation, which undermined the implementation of such policies on time.

The literature notes that political leaders, in particular the then president, Thabo Mbeki, believed that AIDS was a disease of poverty and that there was no link between HIV and AIDS (Schneider & Stein, 2001:728). Consequently, his administration prioritised policies to alleviate poverty. This resulted in the rejection of antiretroviral drugs which had been scientifically proven effective. Instead, the administration implemented scandalous measures such as the adoption of chemical compound Viroden instead of antiretroviral therapy. The refusal to provide antiretroviral treatment to HIV-infected pregnant women and other adults was justified in terms of non-affordability and the side effects of the drugs. The

provision of antiretrovirals to patients who needed them was forced on government through pressure and court action on the part of activists and civil society. In 2003, the public sector started making antiretroviral drugs available to patients (Department of Health, 2003a).

The unwillingness of the government to provide antiretroviral drugs meant that patients' coverage was slower than planned (Nattrass & Geffen, 2005:65). The refusal to providing antiretrovirals and the slow pace of rollout resulted in an unprecedented burden of HIV/AIDS. It is documented that the government's failure to act appropriately resulted in hundreds of thousands of deaths which could have been avoided during the period 2000-2005 (Chigwedere *et al.*, 2008). The failure of the government to act on time also resulted in an exponential increase in the infection rate from 0.8% in 1990 to 30.2% in 2005 and an increase in the number of people infected with HIV from 50,000 in 1990 to 4 million in 2005 (Nyabadza *et al.*, 2010).

This situation changed in 2007. The Jacob Zuma administration committed itself to the implementation of SANAC's five-year, 2007-2011, strategic plan. The government urged every South African to be responsible by testing freely at South African clinics on a regular basis in order to receive treatment. Furthermore, the government campaigned against stigma and discrimination through a door-to-door campaign, billboard messages and vox pops, and set a target to test 15 million people by June 2010 (Culliman & Bodibe, 2010). In 2009, President Zuma announced generous policies in favour of the most vulnerable sections of the population. These included the provision of antiretroviral treatment to children under the age of one who test HIV-positive and earlier ARV (at CD4 count 350) to pregnant women and patients with TB and AIDS co-infection (Govender, 2009). In 2011, earlier treatment was expanded to everyone who qualifies. On the facility side, managerial and attitudinal deficiencies in district-level health care facilities were addressed. In terms of funding, the HIV/AIDS budget was increased by 33% between 2009 and 2010; and in 2011, it was further increased by 30% (Motsoaledi, 2011).

3.2 Extent of HIV/AIDS interventions' effectiveness

Despite the efforts of the South African Government to improve the response to HIV/AIDS and the resulting effectiveness in terms of reduced infections and deaths, the effectiveness in terms of patients reached remains limited. This limitation arises from a shortage of resources which do not grow on par with the growth in the number of patients. While progressive HIV/AIDS policies have been adopted since 2007, the shortage of resources can compromise the future effectiveness of HIV/AIDS interventions in terms of coverage if the levels of risky behaviours do not change significantly.

3.2.1 Past and recent past

The government's late response to HIV/AIDS resulted in a huge burden of the epidemic. This limited the effectiveness of HIV/AIDS interventions in terms of patients reached despite an increase in funding.

HIV/AIDS funding in South Africa can be understood by examining trends in HIV/AIDS conditional grants to provincial and local government. These conditional grants, which increased over time, were channelled to HIV/AIDS through three social sector departments; the Department of Health which is mainly responsible for HIV/AIDS care, the Department of Social Development which is responsible for HIV/AIDS social programmes and the Department of Education which is responsible for HIV/AIDS life skills. Table 3:2 shows that HIV/AIDS funding has increased over time.

Table 3:2 Government HIV/AIDS funding in South Africa (in thousands of Rands, current prices)

Programme	2005/2006	2006/2007	2007/2008	2008/2009	MTE2009/2010*	MTEF2010/2011	MTEF 2011/2012
Education HIV and AIDS allocations (life skills education grants)	136,300	144,500	157, 600	171,100	177,400	188,000	199,300
Social Development HIV and AIDS allocations (National & Provincial Allocations)	233,337	280,547	409,016	478,891	564,986	669,152	709,298
Health HIV and AIDS allocations (National, Conditional Grants & Provincial Discretionary)	2,076,041	2,681,623	3,537,471	4,304,436	5,929,599	5, 997,856	6,472,633
Total national HIV and AIDS related social sector budgets	2,445,678	3,106,670	4,104,087	4,954,427	6,671,985	6,855,008	7,381,231

Source: Adapted from Ndlovu (2009:25).

* MTEF is the Medium Term Expenditure Framework in which the government plans expenditure and revenue for the next three years

This increase in funding permitted an expansion of HIV/AIDS interventions and resulted in an increase in the effectiveness of these interventions in terms of patient coverage. Increased investment in mass education campaigns notably Soul City for adults, Soul Buddyz for children, Love Life for teenagers (HSRC/MRC/CADRE, 2009,) and more recently VCT campaigns (SANAC, 2010 b), resulted in increased exposure to these interventions. The HSRC/MRC/CADRE (2009) reported an increase in exposure to these programmes from 75% in 2005 to 80% in 2008. In terms of treatment interventions, South Africa significantly increased access to HAART. In 2012, the country reached the target of universal treatment. It is reported that in 2012, 80% or 2 million patients out of 2.4 million in need of HAART were receiving it (IRIN/Plus News, 2012).

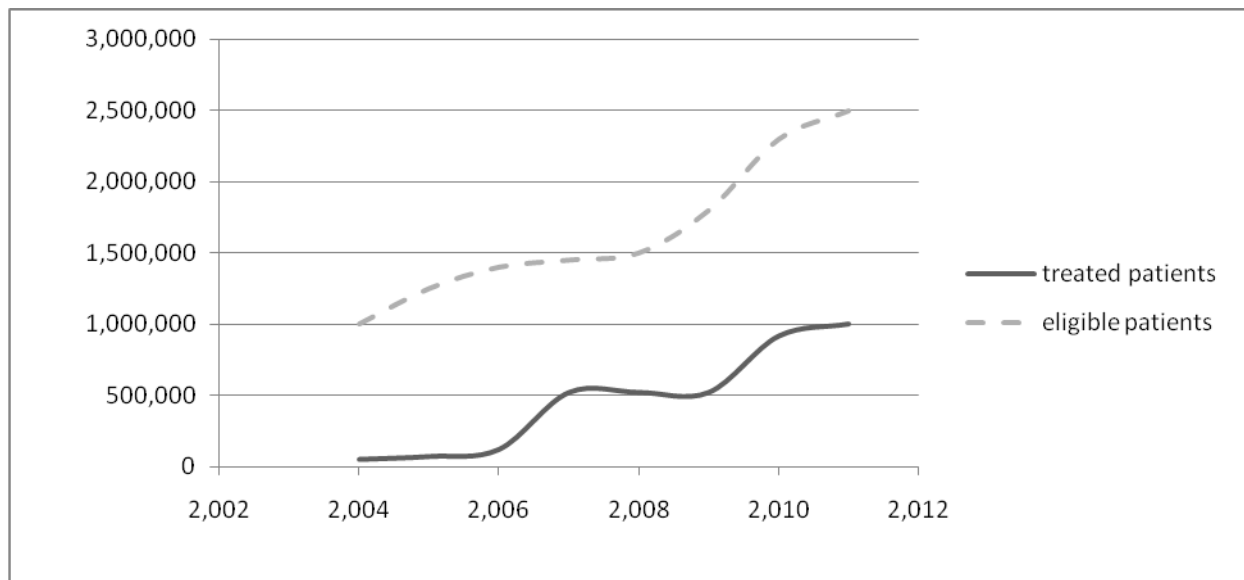
For patients reached by HIV/AIDS interventions, effectiveness in terms of a reduction of suffering and death increased. The scale-up of the antiretroviral programme led to a significant decrease in morbidity and mortality (Dorrington, 2011). Likewise, patients reached by prevention interventions decreased their risky behaviours. In 2008, a survey revealed that mass information campaigns had generally decreased risky sexual behaviours among adults (HSRC/MRC/CADRE, 2009); Govender's (2011) study on the impact of Soul City confirmed these results. It has also been widely documented that as a result of an increase in the coverage of prevention interventions, condom usage increased and the number of sexual partners decreased (Shisana & Simbayi, 2002; HSRC 2005; 2009; Williams, 2003, Pettifor *et al.*, 2004; Pronyk *et al.*, 2008; Pronyk *et al.*, 2006).

However, an increase in funding does not imply effectiveness in terms of patients reached as demand-side factors may play a deleterious role. While the increase in funding increased access to HIV/AIDS interventions, other evidence indicates that many patients are still unable to access HIV/AIDS interventions. The limited extent of effectiveness in terms of how HIV/AIDS interventions reach prospective patients is illustrated by low exposure to one of the most important interventions in South Africa, VCT. In 2011, Walensky *et al.* (2011: 26) found that more than 3 out of 5 million people infected are unaware of their HIV status and that only 47% of all

South Africans and 34% of those infected reported that they had tested for HIV. Pitpitan *et al.* (2012) found that only 49% of South Africans have ever tested for HIV. As the effectiveness of HIV/AIDS interventions begins with reaching those in need, this evidence suggests that their effectiveness in South Africa is still limited.

Another issue is the extent to which accessing HIV/AIDS interventions or decreasing risky behaviours translates into actual reduction in infection rates. Many other factors such as sexual partners' biological conditions may influence the infection rate more than behaviour. The evidence indicates that females are more at risk than male because of the efficiency of the transmission of the virus from a male to female (Nicolosi *et al.*, 1994). Therefore, a woman who reduces her risky behaviour as a result of an intervention is still more likely to be infected than a man who did not reduce his risky behaviour. This has resulted in inconclusive research findings on the effectiveness of HIV/AIDS behavioural prevention interventions. Studies that have reviewed interventions in South Africa have hesitated to draw firm conclusions about which intervention works best in terms of reducing infections (Harrison, 2010; Harrison *et al.*, 2010).

While the effectiveness of HAART in changing health outcomes in South Africa has been acknowledged (Fairall, 2008; Dorrington, 2011), until the end of 2011 the intervention had not reached many patients in need. Even with a significant increase in patients accessing treatment in 2012, many patients (20%) do not access treatment. The difference between intervention services and patients in need can be grasped by examining the gap between eligible and treated patients; this is shown in Figure 3:1.



Sources: Data obtained from Adam & Johnson (2009) and Meyer-Rath (2010).

Figure 3:1 Comparison of eligible and treated patients since the launch of ARV treatment

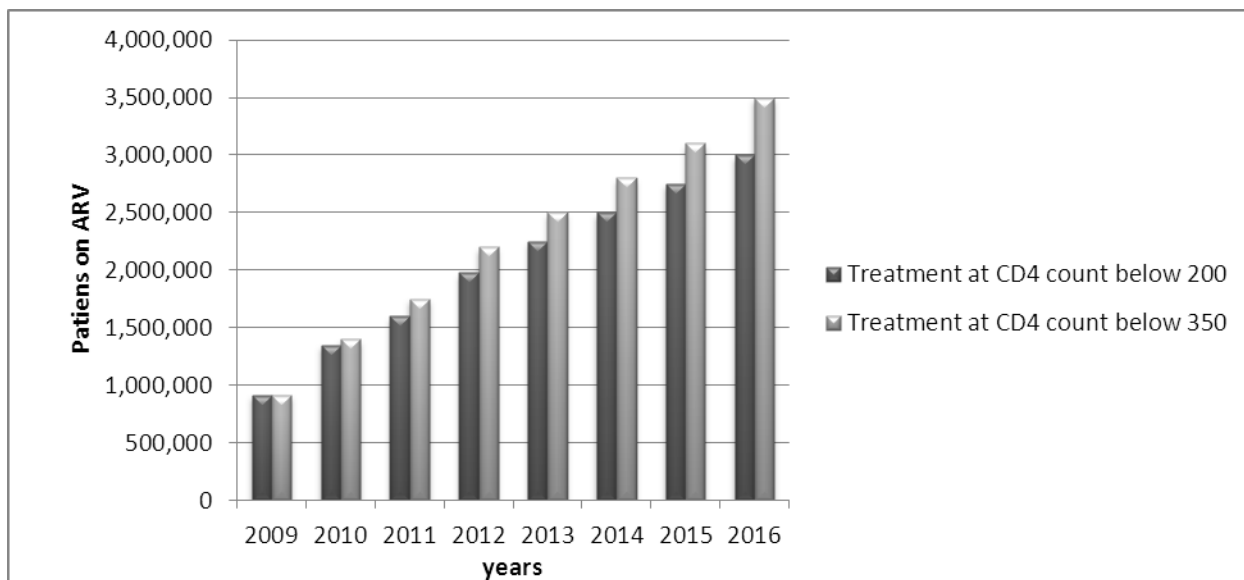
Figure 3:1 shows that since 2009, the gap between eligible and treated patients has been almost the same as in previous years. The gap in 2009 persisted or increased when the number of eligible patients increased, suggesting that additional funding served less additional eligible patients.

The funding shortfall highlighted above has also been documented with regard to treatment affordability in terms of the number of untreated but eligible patients (Mills, 2008), shortage of infrastructure, and human resources. A 2008 study estimated that about 900,000 eligible (on the basis of CD4 counts 200 threshold or the World Health Organisation stage 4) adults were not on treatment. The same study estimated that only 40.2% of all eligible patients were treated in 2008, although this was a huge increase from 4.9% in 2004 (Adam & Johnson, 2009:661). Limited effectiveness also manifested in terms of the limited number of antiretroviral drugs provision facilities (Meyer-Rath, 2010), although this may also be a result of poor planning. The extent of effectiveness in terms of patients reached by HAART interventions is likely to be even more limited with more recent commitments on the part of the South African Government.

3.2.2 Future prospects

The above limitations of the effectiveness of HIV/AIDS interventions in observed data are likely to persist in the future. Indeed, government's increased commitment to enrol patients on HAART on a universal basis raises the question of whether or not funding will be available in the future. A simplistic analysis would predict a funding shortfall, given an immediate increase in the number of eligible patients. A more realistic analysis, however, would take into account the longer term savings in terms of avoided opportunistic and new HIV infections and the likely decrease in the cost of ARV drugs (Bangsberg *et al.*, 2001).

The funding shortfall analysis in South Africa should take into account the increase in the number of patients as well as the cost savings emanating from early treatment in order to estimate the additional funding requirement. In this respect, one study projected that with early treatment, the number of patients over the period 2010-2016 would increase. Figure 3:2 shows these data.



Sources: adapted from Meyer-Rath (2010)

Figure 3:2 Projected trends in patients who would be on ARV therapy at treatment thresholds of 200 and 350 CD4 counts: South Africa

The results depicted in Figure 3:2 show that early treatment would increase the number of patients from 900,000 in 2009 to 3,500,000 in 2016 (an increase of 288%), 14% more than late treatment, which would increase the number of patients from 900,000 in 2009 to 3,000,000 in 2016 (233%) as shown in Figure 3:2. Over the same period, it is estimated that the costs of early treatment would be about R70 billion, 17% more than the cost of late treatment of R59 billion (Meyer-Rath, 2010), which would be exorbitant if one considers the available government funding in Table 3:2. A more recent study (Hontelez *et al.*, 2011) that analysed universal early treatment (at CD4 counts of 350) projected significantly greater benefits with modestly higher costs, which would break even with the costs of late treatment by 2026.

Whether or not this long-term prediction will turn out to be true, the limitations of the extent of HIV/AIDS interventions relate mainly to the short-term. In light of the situation in the recent past, it could be argued that government will likely suffer a shortage of funds. Indeed, following the announcement of the early treatment of pregnant women and children in 2009, the number of eligible patients increased more (50%) than the increase in funding (30%) over previous years (Adam & Johnson, 2009).

While these studies suggest that long-term effectiveness might not be a concern, short-term funding prospects remain a challenge. Increasing funding in order to provide early treatment to eligible patients would require a significant increase in revenue. However, the extent to which the country can increase its main source of revenue, tax revenue, to fund early HIV/AIDS treatment is limited in the context of 2012 and subsequent years' economic prospects. Increasing revenue will require an increase in tax rates and /or an increase in taxable income. While an increase in tax rates might have a deleterious effect on economic activity, an increase in taxable income will be difficult to achieve given the effects of the global economic slowdown and the financial crisis in Europe, which is South Africa's main export market. The

economy has not created sufficient jobs or business opportunities and the chances of this situation changing in the near future are slim. Slow economic growth leads to increasing poverty and the need for an increase in social security. HIV/AIDS interventions are therefore likely to compete for funds with poverty related social programmes such as social spending and education. The country needed about R104 billion (about US\$13 billion) for the 2011/2012 fiscal year to cater for the 16 million people in need of social grants (Hweshe, 2011).

The current health care system in South Africa also contributes to the limitation of the effectiveness of HIV/AIDS interventions by only reaching a restricted number of patients. The system serves fewer people in need because most of those affected by HIV/AIDS are poor and rely on the services of the public sector. However, the public sector's resources are not commensurate with the number of HIV/AIDS patients it is supposed to serve. A national health insurance system is expected to resolve this problem by allowing people access to HIV/AIDS services regardless of their ability to pay, but controversy still surrounds its affordability (Parker, 2010). Consequently the effectiveness of HIV/AIDS interventions will remain limited in terms of patients' access to services.

Non-economic factors such as stigma which remains persistent in South Africa (Mahajan *et al.*, 2008, Campbell *et al.*, 2005), also cast doubt on the future effectiveness of HIV/AIDS interventions with respect to the number of patients reached. Despite the widespread incidence of HIV/AIDS, stigma is still reported to be an important deterrent to accessing HIV/AIDS interventions or to adhering to treatment (Young *et al.*, 2010). If stigma persists, it will limit the effectiveness in terms of the number of patients reached by interventions and their health status. Non-adherence as a result of stigma leads to an increase in opportunistic infections and the development of drug resistance, both of which aggravate health status (Bangsberg *et al.*, 2001).

Briefly, the discussion in this section indicates that the effectiveness of HIV/AIDS interventions in South Africa has remained limited and requires improvement in

policy implementation. The next section discusses the extent to which these policies have been implemented in South Africa.

3.3 Effectiveness-targeted policies

Policies to increase the effectiveness of HIV/AIDS interventions in South Africa have failed to address both the supply-side and demand-side factors. This has reduced the effectiveness of HIV/AIDS interventions.

3.3.1 Supply-side policies

South Africa put supply-side policies in place to improve the effectiveness of HIV/AIDS interventions. Broadly, these policies consisted of strategies to supply HIV/AIDS services in the country. Formulated since 2000, the strategies were imbedded in successive five-year strategic plans which determined the priority of HIV/AIDS interventions and how they had to be conducted. An important aspect of these strategic plans was involving many stakeholders in the response to HIV/AIDS because of its multifaceted nature. The responses arising from the plans resulted in an improvement in resource allocation and effectiveness in terms of coverage. Supply-side policies focused on addressing factors that limit access to HIV/AIDS services, such as a shortage of resources, HIV/AIDS facilities, drugs and human resources (Ndlovu, 2009), political unwillingness (Roger, 2009) and inadequate linkage of prevention to care (Bhagwanjee *et al.*, 2008)

Since 2012, policies to improve the effectiveness of HIV/AIDS interventions through supply-side factors included negotiations to decrease drug prices (Lucchini *et al.*, 2007: 174)). Other policy options included successful implementation of plans to manufacture some of the antiretroviral drugs locally (*Business Report*, 2012). More effective interventions such as PMTCT and HAART have been prioritised and more resources have been earmarked for them. Services have been made more widespread in order to reduce demand costs in terms of transport fares.

At the implementation stage however, failure to improve effectiveness has resulted from government's inability to fulfil its coordinating role. For instance, the government did not sufficiently mobilise the community around HIV/AIDS; such mobilisation has been found to increase effectiveness elsewhere (Oster, 2007). Community mobilisation could have raised responsibility among community members to deal with the epidemic. In particular, community mobilisation would have shifted some HIV/AIDS tasks from medical staff to members of the community and taken advantage of the empirical benefits of such a shift (Schneider *et al.*, 2008). Inadequacy in mobilising the community resulted in fewer patients being reached.

3.3.2 Demand-side policies

Supply-side deficiencies in policy making deterred the demand for HIV/AIDS services. The political attitude in the early 2000s created negative perceptions among the population about the benefits of HIV/AIDS services. A recent study cited political equivocation as one of the deterrents to the demand for antiretroviral services (Mills, 2008). This political equivocation left its mark on the mind-set of the population to the extent that many people still may not believe in the benefits of the HIV/AIDS interventions provided by the government.

Supply management as a deterrent to demand for HIV/AIDS services was also manifested in the provision of services. The literature in Southern Africa indicates that the low morale of medical staff as a result of the burden of patients (Zelinick & O'Donnell, 2005) led to a deterioration of services, so that there was less patient demand for such services (Pendukeni; 2004, USAID, 2005). Another study indicated that the negative attitude of health care personnel towards HIV/AIDS patients played a role in deterring demand for HIV/AIDS services (Yeap *et al.*, 2010). Policy to deal with this has been limited to regulations but the extent to which these regulations have been implemented has not been clarified.

Virus resistance and drug side-effects have been reported as deterrents to demand for HIV/AIDS services and can only be dealt with by services supply management

(Yeap *et al.*, 2010). It is not clear how South African policy has responded to virus resistance and side-effects. This also applies to the management of serious HIV and TB co-infections. Some policies have been formulated to reduce the impact of co-infections but the fact that high mortality as a result of HIV and TB co-infection persists (O'Donnell *et al.*, 2013) implies that the policy has had little effect at the implementation stage.

Poverty, one of the community level factors, is also likely to reduce the effectiveness of HIV/AIDS interventions. Poverty has been a deterrent to the use of HIV/AIDS services due to hopelessness. Policy to deal with poverty has mainly consisted of distributing social grants. However poverty is associated with many other factors such as health illiteracy, multiple relationships, gender violence, substance abuse, crime and stigma which have been shown to perpetuate infections (Gouws, 2010). A study by Kagee (2006) in Cape Town suggested that psychosocial factors such as stigma affect individual-level demand for HIV/AIDS services. Campaigns against stigma have been launched recently (Culliman, K. & Bodibe, 2010), but their effectiveness has not yet been demonstrated.

Briefly, the above analysis shows that official policy has focused more on supply-side than demand-side factors. Furthermore, both supply-side and demand-side policies have not been implemented adequately and as a result the effectiveness of HIV/AIDS interventions has been limited. Another weakness in HIV/AIDS policy concerns the absence of context-specific policies to improve the effectiveness of HIV/AIDS interventions.

3.4 Context-specific HIV/AIDS policies

Since epidemiological and socio-economic contexts in South Africa abound with demand-side factors in different patterns and to different extents, some policy strategies could have worked better in some contexts than in others. This suggests that context-specific policies would have improved the effectiveness of HIV/AIDS interventions in South Africa.

Context-dependent HIV/AIDS response policy recommendations have been addressed in the literature for some time (Grassly *et al.*, 2001:1121). The rationale is that an HIV/AIDS intervention can have different success rates, depending on where it is implemented. Indeed, the extent to which an intervention succeeds depends on its net effect, between the risk factors and its own effect in reducing the impact. Risk factors are diverse, and range from structural factors (Pronyk *et al.*, 2006; Pronyk *et al.*, 2008; Raogupta *et al.*, 2008) to epidemiological factors (Geoffard & Phillipson, 1996), environmental factors (Bolton & Talman, 2010) and cultural factors (Airhihenbuwa, 2004). Risk factors have been found to influence health theoretically and empirically through their influence on health-seeking behaviour and attitudes towards health interventions (Bandura, 1986; Becker, 1974; Geoffard & Phillipson, 1996) and their linkage with culture (Airhihenbuwa, 2004). They are consequently expected to be at the centre stage of the differences in new infections, sickness and deaths, even in the presence of HIV/AIDS interventions. Finding policy responses which deal most appropriately with the parameters of a given context would therefore contribute to greater effectiveness.

South Africa is good terrain for context-specific policy in relation to HIV/AIDS interventions. The country has a relatively low HIV prevalence context and a relatively high prevalence context as defined in this study. South Africa is also characterised by stark differences in socio-economic contexts with a very poor rural context and a relatively well-off urban context. Policy response tailored to the realities in these contexts would improve effectiveness.

Despite the country being good terrain for contextual response to HIV/AIDS, this has not been addressed by the policy process. South Africa has adopted a uniform response to HIV/AIDS regardless of the differentiated impact across an LPC and a HPC and across a rural context and an urban context. The response to HIV/AIDS in South Africa has taken no account of the fact that factors influencing the effectiveness of HIV/AIDS interventions may be specific to these contexts. It has mainly ignored the fact that the difference in the factors might underlie observed

differentials in the impact of HIV/AIDS which may persist if HIV/AIDS interventions are conducted uniformly regardless of contextualisation.

Contextual HIV/AIDS policy responses in South Africa have addressed the context of patients such as gender and age rather than broad geographical contexts. For instance, pregnant mothers and children were considered the most vulnerable and contextually different from other groups of patients. The policy response to deal with such vulnerability and which improved effectiveness consisted of starting them on HAART earlier than other patients. In the same vein, patients co-infected with HIV and TB were seen as contextually different in terms of vulnerability and effectiveness in their treatment was improved by giving them HAART regardless of their CD4 counts (Govender, 2009). Targeting the most vulnerable patients such the youth aged 14-24 to increase the effectiveness of interventions in the general population has been the norm in other countries. For instance, studies have found that it is important to stop infections in women (Laga *et al.*, 2001; Sterling *et al.*, 2008; Gouws & Abdool Karim, 2010: 56) and youth aged 15-24 (Ross *et al.*, 2010) to improve effectiveness in Africa.

While it has commonly been argued that the effectiveness of HIV/AIDS interventions may depend on contexts, geographical context-specific policies have been absent in South Africa. This study argues that more effectiveness could have been achieved by designing more contextual responses. The rationale for this argument is that if HIV/AIDS policy responses are tailored to all contextual groups of patients, an appropriate policy response tailored to geographical and socio-economic contexts would have been included to improved effectiveness. Both demand-side and supply-side policies have not been very effective because their implementation has not been context-specific, yet HIV/AIDS in South Africa has both epidemiological and socio-economic contexts.

Chapter summary

This chapter reviewed HIV/AIDS interventions in South Africa with the aim of establishing the extent to which these have been context-specific. It was noted that effectiveness in terms of coverage and health outcomes has improved over time but there appears to be much room for improvement. One way to improve effectiveness is to design geographical and socio-economic context-specific responses. However, as the review showed, the extent of such responses has been limited. Although the consideration of the effectiveness of HIV/AIDS interventions is one aspect of policy making, the joint consideration of cost and effectiveness is an even more important aspect of the policy process. The extent to which the joint evidence on cost and effectiveness has been available to policy makers is the subject of the next chapter.

Chapter 4 : Cost-effectiveness studies of HIV/AIDS interventions in South Africa

This chapter reviews CE studies of HIV/AIDS interventions in South Africa in order to identify the gaps in contextual cost-effectiveness analysis. Section one presents an overview of CE studies. Section two analyses the extent of CE studies through their patterns. Section three assesses whether or not the most relevant CE evidence for the country has been made available to policy makers, while section four assesses the extent of CE studies of HIV/AIDS interventions across contexts.

4.1 CE studies of HIV/AIDS interventions in South Africa: An overview

Thirty distinct CE studies in the public domain were obtained through a search of databases for the period 1995-2012. This section discusses the evolution of CE studies as well as the conduct of these studies with a view to identifying gaps in relation to contextual cost-effectiveness analysis.

4.1.1 Evolution of CE studies in South Africa

CE studies evolved over time in line with the change in the response to HIV/AIDS. This evolution is discussed per category of intervention notably (1) treatment and care (2) biomedical prevention and (3) behavioural prevention² and per date of the study.

4.1.1.1 Treatment and care interventions

The earliest CE studies of HIV/AIDS interventions in South Africa were in the category of treatment and care interventions, which consisted of non-HAART interventions and HAART interventions. The non-HAART studies are shown in Table 4:1.

² This resulted in 35 CE comparisons because some studies covered more than one category of interventions.

Table 4:1 Summary of CE studies of non-HAART interventions in South Africa

Evolution of CE studies		Methodological features			Citation, comparison number and study number ³
Study area	Options compared	Follow-up	Results	Recommendation	
Cape Town no-isoniazid among TB infected stratified by HIV/AIDS status (0) isoniazid (1)		Hypothetical population of 100,000 HIV-positive people modelled using a spread sheet	Isoniazid is cost saving, saving R40.6 million over 8 years period	Obvious that isoniazid is the better option than no isoniazid and does not require value judgment.	Masobe <i>et al.</i> (1995), (1), (1)
Cape town Pro-test package (0) no Pro-test package (1)		The costs were estimated based on ingredient method for facility participating.	The cost-per HIV infection averted by VCT range was US\$67-US\$112, the cost per TB case prevented by VCT range was US\$129-US\$215 for normal VCT and US\$323-US\$664 for intensified case finding.	Pro-test was cost saving.	Hausler <i>et al.</i> (2006) (2), (2)
South Africa No isoniazid (0) late isoniazid(1) early isoniazid (2) late isoniazid and cotrimoxazole(4) late cotrimoxazole(5) early isoniazid +cotrimoxazole(6) early cotrimoxazole (7)		Hypothetical population modelled using Markov modelling	Incremental costs per life year gained of (1) to (7) over (0) are US\$-430,US\$170,US\$17,US\$779,US\$244,& US\$1104	CE judged on basis of the national per capita income.	Bachmann (2006) (3), (3)
No STD (0), STD (1) PMTCT (2)		Used the projections of the ASSA AIDS model	Direct costs of combined intervention in 2015 would be R20 billion	Low net cost to government given orphanhood, and opportunistic infections costs saved	Geffen <i>et al.</i> (2003) (4), (4)
Hillbrow, Johannesburg syndromic management with no periodic presumptive treatment, PPT (0), syndromic management with PPT (1)		Used hypothetical cohort and a mathematical model	CE was US\$78/ DALY averted. ICER of PPT was US\$31/DALY averted. Initiating PPT at 15% prevalence level would have improved CE by 35%	Interventions targeted at HIV prevalence are CE at all HIV stages. PPT could improve the CE of targeted STI interventions.	(5), (5) Vickerman (2006)

³ The first and second number of each study in the 5th column of the Table denotes the study comparison and the study count respectively. There are more comparisons than studies because some studies made comparisons which spanned different categories of interventions. The study comparisons and count are numbered consecutively from the first Table in section 4.1.1.

The table shows that the earliest CE study in this category was a study of non-HAART interventions by Masobe *et al.* (1995). This study compared no provision of isoniazid (0) with provision of isoniazid (1) among TB patients stratified by HIV/AIDS status in Cape Town. The main result of the study was that isoniazid saved R40.8 million (about US\$4.08 million) in costs over an eight-year period. This study was followed by Hausler *et al.*'s (2006) study in Cape Town which compared a no Pro-test package (0) with a Pro-test package (1). The Pro-test package, recommended by the World Health Organisation for countries with high HIV/AIDS and TB prevalence, included voluntary counselling and testing, screening for TB through intensified case findings and provision of isoniazid and cotrimoxazole to HIV/AIDS patients to prevent TB. The study's results were that the cost per HIV and TB infection prevented by no Pro-test Package (0) ranged between US\$67 and US\$129 and that the cost per HIV and TB infection averted by Pro-test Package (1) ranged between US\$112 and US\$212. Bachmann (2006)'s study in this category compared options to prevent TB with the provision of isoniazid⁴ and cotrimoxazole to TB and HIV/AIDS patients even though the study included CE comparisons of HAART. The incremental cost per life-year gained for various options compared with no isoniazid (0) ranged from US\$17 to US\$1,104.

Up to 2003, the CE of treating sexually transmitted infections had not been estimated. Geffen *et al.* (2003) was the first study to carry out such estimation. Evaluating the costs and health outcomes of the intervention alongside the costs and health outcomes of VCT, PMTCT and HAART, the study estimated that by the year 2015, these interventions would cost up to R20 billion (about US\$2 billion). While this study evaluated the CE of the intervention alongside other interventions, specific CE evidence on treating sexually transmitted infections was provided by Vickerman *et al.* (2006 a). This study compared the CE of syndromic management with no periodic presumptive treatment (0) and syndromic management with periodic presumptive treatment (1). In this study, STIs were treated in one group of patients based on observed symptoms for every period of treatment, and on

⁴ Isoniazid is an antibiotic used to treat tuberculosis by killing the bacteria which cause the disease while cotrimoxazole eliminates bacteria that cause various infections. In the context of HIV/AIDS, these antibiotics are used to minimize the chances of opportunistic infections.

presumed symptoms in another group of patients. The study reported that the additional cost per DALY averted by syndromic management with periodic presumptive treatment (1) was US\$31. It concluded that syndromic management with periodic presumptive treatment (1) was cost-effective. The study further observed that targeting syndromic management with periodic presumptive treatment (1) at higher HIV prevalence levels would improve the CE of the intervention.

While the CE study of non-HAART dates back to 1995, the first CE study of HAART interventions appeared in the early to mid-2000s. Table 4:2 shows the data.

Table 4:2 Summary of CE studies of HAART in South Africa up to 2005

Evolution of CE studies	Methodological features			Citation, analysis number and study number ⁵
Study area	Follow-up	Results	Recommendation	
Options compared				
Baseline (generic medication, baseline testing and visit costs (1), Higher proportion of doctors' visits (2), patent medicine pricing scenario (3), second line treatment offered to 50% (4), combination of scenarios 2 and 3 (5) second line treatment to 75% with scenario 2, 3 and 4 (6), scenario 2 and 4, (7), scenario 2,3, 4 (8)	The population was hypothetically modelled using a spread sheet model. Parameters from Western Cape Médecins Sans Frontières cohort studies	Cost per life year gained is R5,923 (US\$908) to R11,829 (US\$1,814)	Concluded that rationed provision of antiretrovirals was affordable and beneficial.	Boulle <i>et al.</i> (2002) (6), (6)
South Africa No HAART(0) HAART (1)	Used the AIDS model of the Actuarial Society of South Africa	Direct costs of combined intervention in 2015 would be R20 billion	Low net cost to government given orphanhood, and opportunistic infections costs saved	Geffen <i>et al.</i> (2003) (7) (7)
Cape Town No HAART and thus treating opportunistic infections (0) HAART(1)	Hypothetical population similar to the population of patients in three dedicated clinics in Khayelitsha modelled with Markov model	HAART cost R13,754 per QALY gained; no HAART cost R14,189 per QALY gained The incremental cost per QALY gained on HAART was R13,621. Lifetime costs were however significant	ART is efficient in economic terms and should be pursued if economically feasible and desirable to society.	Cleary <i>et al.</i> (2004) (8) , (7)
South Africa: Prevention only (0) HAART linked to prevention in the case of reduced price (1)	AIDS model of the Actuarial Society of South Africa	Decrease in risk behaviours and infectivity reduction for those on treatment make treatment linked to prevention more advantageous	Large scale comprehensive (prevention and treatment) is advantageous.	Nattrass & Geffen (2005) (10), (9)

⁵ The first and second number of each study in the 5th column of the Table denotes the study comparison and the study count respectively. There are more comparisons than studies because some studies made comparisons which spanned different categories of interventions. The study comparisons and count are numbered consecutively from the first Table in section 4.1.1.

Table 4:2 shows that earlier studies on the CE of HAART focused on comparing HAART versus no HAART. Boulle *et al.* (2002) was the first study in this category. This study compared eight different scenarios of providing antiretroviral drugs to a limited segment (10%) of the adult HIV/AIDS population in South Africa. It examined the scenarios of changing the type of antiretroviral drugs, the number of doctors' visits, proportion of patients receiving second line drugs, and some combination of these scenarios. The cost per life-year gained by each scenario over the others ranged from US\$908 to US\$1,814.

Geffen *et al.* (2003) provided the next study which evaluated the costs and health benefits of HAART although the evaluation included other major HIV/AIDS interventions, notably VCT, STD, and PMTCT. The study projected the direct costs of HAART and other interventions at R20 billion (about US\$2 billion) by the year 2015.

As cohort data on cost and effectiveness of HAART became available from pilot facilities in Cape Town, CE studies comparing HAART (1) *versus* no HAART (0) used such data (Cleary *et al.*, 2004). The results of the study showed that the incremental cost per QALY gained on HAART was R13, 621 (about US\$1,362). The study concluded that HAART was efficient in economic terms and should be pursued even though it observed that lifetime cost of HAART would be significant.

In this category of studies, Nattrass & Geffen (2005) compared prevention alone (0) and prevention linked to HAART (1) and introduced the effect of the decrease in the price of antiretrovirals in this comparison. The study showed that prevention linked to HAART (1) was cost-effective and argued against prevention alone (0), which had been advocated for developing countries (Marseille *et al.*, 2002).

CE studies using pilot sites data and modelling to compare HAART (1) *versus* no HAART (0) continued after 2005 as shown in Table 4.3 (Cleary *et al.*, 2006; Badri *et al.*, 2006).

Table 4:3 Summary of CE studies of HAART in South Africa after 2005

Evolution of CE studies		Methodological features			Citation, analysis number and study number ⁶
Study area	Options compared	Follow-up	Results	Recommendation	
Cape Town: No HAAR(0), HAART (1)		Hypothetical population was used and compared using evidence from Médecins Sans Frontières	Cost per QALY gained of ARV over non ARV was US\$1,102 per QALY gained and US\$984 per life year gained	Concluded that HAART is cost-effective.	Cleary <i>et al.</i> (2006) (13), (11)
Cape Town: No HAART(0) HAARR (1)		Followed up patients in Cape Town AIDS cohort patients	Incremental cost per life year gained from HAART over no HAART was US\$1,342 per patient year under current pricing scenario and US\$793 under reduced cost scenario.	HAART was judged cost effective on the basis that each intervention which achieved less than twice per capita income (US\$6,960 at the time of the study in 2004) was cost-effective.	Badri <i>et al.</i> (2006) (9), (8)

One of these studies (Badri *et al.*, 2006) included sensitivity analysis results on pricing scenarios to take into account anticipated trends in the decrease in drug prices at the time. Cleary *et al.*'s (2006) study found that the incremental cost per QALY gained by HAART intervention (1) compared with no HAART (0) was R13,624 (about US\$ 1,362) while Badri *et al.* (2006) reported that the incremental cost per life year gained by HAART intervention (1) compared with no HAART (0) was US\$1,342.

Another type of CE comparison, CE comparison of HAART timing, emerged in 2006 as shown in Table 4.4.

⁶ The first and second number of each study in the 5th column of the Table denotes the study comparison and the study count respectively. There are more comparisons than studies because some studies made comparisons which spanned different categories of interventions. The study comparisons and count are numbered consecutively from the first Table in section 4.1.1.

Table 4:4 Summary of CE studies of timing of HAART interventions in South Africa

Evolution of CE studies	Methodological features			Citation, analysis number and study number ⁷
	Study area	Follow-up	Results	
Options compared				
South Africa: No intervention (0) Early ARV (1) Late ARV (2)	The population was hypothetically modelled using Markov model	ICER of (1) and (2) over (0) is US\$2,817 and US\$2,443 per QALY gained	CE on per capita income threshold.	Bachmann (2006) (11)
Cape Town No HAART(0), Initiating HAART at CD4 count 200(1), initiating HAART at CD4 between 200-50 (2), and initiating HAART at CD4 count above 350 (3)	Hypothetical patients modelled using Markov model	HAART at CD4 200 had ICER of US\$54/QALY over no HAART; HAART at CD4 200-350 had an ICER of US \$616 over HAART at CD4 count 200; HAART at CD4 count >350 had an ICER of US\$1,137 over HAART at CD4 count 200-350	Concluded that HAART is generally cost-effective and more effective when initiated earlier.	Badri <i>et al.</i> (2006) (12), (10)

One of these studies, Bachmann (2006), compared the CE of starting treatment early (1), that is, at a CD count threshold of 350 and starting treatment late (2), that is, at a CD4 count threshold of 200. The study found that, relative to no treatment (0), the incremental cost per QALY gained was US\$2,817 for starting treatment early (1) and the incremental cost per QALY gained was US\$2,443 for starting treatment late (2). The study argued that early timing and late timing of treatment were both cost-effective. Therefore, even late treatment is better than no treatment.

Badri *et al.* (2006) was a related study which adopted a stratified approach. It analysed the CE of timing of HAART by comparing the CE in several strata of starting treatment. These strata were: starting treatment at a CD4 count threshold of 200 (1), at a CD4 count threshold between 200 and 350 (2), and at a CD4 count

⁷The first and second number of each study in the 5th column of the Table denotes the study comparison and the study count respectively. There are more comparisons than studies because some studies made comparisons which spanned different categories of interventions. The study comparisons and count are numbered consecutively from the first Table in section 4.1.1.

threshold greater than 350 (3), while including no HAART (0) as a baseline intervention. Relative to no HAART (0), the ICER per QALY gained of starting treatment at a CD4 count threshold of 200 (1) was US\$54. Relative to starting treatment at a CD4 count threshold of 200 (1) the ICER per QALY gained of starting treatment at a CD4 count threshold between 200 and 350 (2) was US\$616. Relative to starting treatment at a CD4 count threshold between 200 and 350 (2), the ICER per QALY of starting treatment at a CD4 count threshold greater than 350 (3) was US\$1,132.

As HAART rollout evolved, so did studies to inform policy makers of CE options. From 2008, CE studies started including new analyses as reported in Table 4.5.

Table 4:5 Summary of CE studies of HAART interventions in South Africa since 2008

Evolution of CE studies	Methodological features			Citation, analysis number and study number ⁸
Study area Option compared	Follow-up	Results	Recommendation	
Cape Town: No HAART(0), HAART with first line only(1) HAART with first and second line (2)	Hypothetical population modelled with Markov and data collected from a cohort in Khayelitsha	First line costs US\$795 relative to no HAART, First and second line costs US\$1,625 relative to first line. If the budget is \$10 billion only first line is efficient. If the budget is 10-12 billion (3) is efficient	Concluded that it is important to consider both efficiency and CE to better guide policy makers.	Cleary <i>et al.</i> (2008) (14), (12)
Cape Town: Symptom based strategies (0), CD4-based strategies (1), CD4 and viral load based strategies (2)	Hypothetical population using a simulation model	Monitoring CD4 counts relative to monitoring symptoms resulted in lifetime cost savings of US \$464 per person while increasing life expectancy by 4 months. Monitoring CD4 and viral load had an ICER of US\$5,414 per life year gained over CD4 monitoring	CD4 monitoring relative to symptom based approach is cost saving.	Bendavid <i>et al.</i> (2008) (15), (13)
South Africa: Current screening practice (0), one time screening (1), screening every 5 years (3), annual screening (4)	Hypothetical population modelled using CEPAC model	ICER US\$1,570/QALY for screening every 5 years over current practice ECER of US\$1,720/QALY over current practice.	Annual screening is very cost-effective based on the finding that CER is less than GDP/capita of \$5400.	Walensky <i>et al.</i> (2011) (17), (15)
South Africa Treatment at CD4 count 200 (0), treatment at CD4 count 350 (1), treatment at CD4 count 500 (3), treating at all CD count levels (4)	Used deterministic compartmental model to model the population of South Africa	Compared with current scenario expanding to <500 prevents additional 583,000 new infections in 5 years and 3 million new infections over 40 years	Increasing the provision of ART to <350 may significantly reduce costs while reducing HIV/AIDS burden.	Granich <i>et al.</i> (2012) (16) (14)

Prior to 2008, no CE comparison had assessed the question of the budgetary requirements of each HAART. By comparing no HAART (0), HAART with first line

⁸ The first and second number of each study in the 5th column of the Table denotes the study comparison and the study count respectively. There are more comparisons than studies because some studies made comparisons which spanned different categories of interventions. The study comparisons and count are numbered consecutively from the first Table in section 4.1.1.

only (1), and HAART with first and second line (3) while including budgetary analysis, Cleary *et al.* (2008) contributed to the evidence regarding the effect of the budget on the cost-effectiveness of HIV/AIDS interventions. They showed that with a budget of US\$10 billion, HAART with first line only (1) would be cost-effective while with a budget of between US\$10 and US\$12 billion; HAART with first and second line (3) would be cost-effective.

Other questions regarding HAART concerned inefficiency in screening methods. Bendavid *et al.* (2008) contributed to the evidence in this respect by comparing screening of HIV/AIDS patients for HAART based on symptoms (0), screening based on CD4 counts (1), and screening based on both CD4 counts and viral load (2). They found that relative to screening of HIV/AIDS patients for HAART based on symptoms (0) screening based on CD4 counts (1) resulted in lifetime cost-savings of US\$464 per person while screening based on both CD4 counts and viral load (2) had an ICER of US\$5,414 per life year gained over (1).

The study of the CE of screening for HIV infections is important as it facilitates linking patients to HAART. This first appeared in the literature in 2011. Walensky *et al.* (2011) compared the CE of different options to screen for HIV infection. The comparison included current screening practice (0), one time screening (1), screening every five years (3), and annual screening (4). It study found that the incremental cost per QALY gained of screening every five years and annual screening (4) relative to current screening practice (0), was US\$1,570.

The earlier treatment policy adopted by the South African Government in 2011 stimulated further CE analysis in 2012. Rather than focusing on the benefits of treatment in terms of AIDS and deaths reduction, Granich *et al.* (2012) focused on the preventative benefits of treatment in terms of new infections averted over the short term (5 years) and long term (40 years). The prevention benefits were compared for starting HAART at CD4 count of 200 (0), at CD4 counts of 350 (1), at CD4 counts of 500 (2), and at all levels of CD4 counts (3). The study found that relative to starting HAART at CD4 count of 200 (0), starting HAART at all levels of

CD4 counts (3) prevented an additional new infections of 583,000 over 5 years and 3 million new HIV infections over 40 years.

4.1.1.2 Biomedical prevention interventions

PMTCT emerged earlier in the literature in the biomedical interventions category (PMTCT, HAART prophylaxis, microbicides, and condom usage). The evolution of the CE of PMTCT followed a series of randomised clinical trials in developed and developing countries⁹. These trials had shown that provision of HAART to mother and infant, at specific times during pregnancy and after birth, significantly reduced HIV transmission to the infant (from 66% to 50%). Table 4.6 shows CE studies of PMTCT up to 2000.

⁹ The first trial in this series was the Multi-Centre AIDS Clinical Trials Groups (ACTG 076) conducted in France and the United States. This trial, which involved providing Zidovudine to pregnant women from week 14 until the time of delivery reduced infection by 66%. Participants in the trial were non-breastfeeding women and its relevance to low income countries was limited due to the duration of the therapy (costly at that time) and the fact that the majority of women in low income countries rely on breastfeeding. The efficacy of a shorter trial in Thailand (reduction of infection by 50%) which consisted of Zidovudine twice daily from week 36 of pregnancy and every three hours from the onset of labour until delivery provided hope (Shaffer *et al.*, 1999) but this was still considered unaffordable and not relevant to breastfeeding women. Trials on this type of patient in Cote d ' Ivoire and Burkina Faso (women with an oral regime of Zidovudine twice daily, a single oral dose at the onset of labour and 7 days of Zidovudine twice daily after birth) reduced transmission by 38% (Dabis *et al.*, 1999) while in Uganda, HIVNET012, which consisted of a single dose of Zidovudine to the mother at week 36, a single dose of Nevirapine (NVP) at the onset of labour, a dose of Zidovudine every three hours during labour, and a single dose of nevirapine to the infant 7 days after birth , reduced HIV transmission by 50% (Guay *et al.*, 1999, Jackson & Fleming 2003).

Table 4:6 Summary of CE studies of PMTCT in South Africa up to 2000

Biomedical prevention intervention	Evolution of CE studies	Methodological features			Citation, analysis number and study number ¹⁰
	Study area	Methods	Results	Recommendation	
	Options compared				
PMTCT	A Rural context in KZN: No intervention (0), zidovudine delivered with current infrastructure (1), zidovudine delivered with enhanced infrastructure (2)	Used decision tree and observed data on 842 pregnant women	With no intervention, there would be 6,570 HIV infections, reduced by 15% at total cost of US\$574,825 with (1) and reduced by 47% at total cost of US\$764,901 with (2)	Although the antiretroviral options are cost-effective, the authors concluded they were not affordable.	Wilkinson <i>et al.</i> (1998) (18) (16)
PMTCT	South Africa No intervention (0), formula feeding (FF) recommended from birth (1), FF recommended from 4 months (2), FF recommended from 7 months (3), FF recommended from birth (4), ACTG076 (5), Petra B (7), CDC Thai (6), CDC Thai+FF recommended (7), and CDC Thai +FF supplied (8)	20 000 hypothetical women and used Markov modelling	Low cost and high cost antiretroviral regimen were equally cost-effective and more cost-effective with formula feeding	The options are CE in case of formula feeding and very CE in case of combination of formula feeding and breastfeeding.	Soderlund <i>et al.</i> (1999) (19), (17)
PMTCT	South Africa Based on data from Hlabisa, KZN No PMTCT(0), short course oral Zidovudine with enhanced infrastructure (1)	Modified a model in Hlabisa to reflect reality of each province in South Africa	Without interventions, 63,397 infections would occur. These infections would be averted at a cost of R155.9 million in 1997	The recommendation is based on the results of other empirical studies on other health interventions such as immunization and family planning.	Wilkinson <i>et al.</i> (2000) (21), (19)
PMTCT	South Africa no intervention (0), 25% mother and infant receive HAART over 2000-2005 (1), 75% receive HAART (2), 100% receive HAART (3)	Produced population projection using the SPMS model.	110, 000 HIV-positive births could be prevented by a short course of antiretrovirals	Barriers to widespread ARV use led the authors to recommend limited use of ARV.	Wood <i>et al.</i> (2000) (20), (18)

¹⁰ The first and second number of each study in the 5th column of the Table denotes the study comparison and the study count respectively. There are more comparisons than studies because some studies made comparisons which spanned different categories of interventions. The study comparisons and count are numbered consecutively from the first Table in section 4.1.1.

The study by Wilkinson *et al.* (1998), which was the first to compare the CE of some PMTCT trial options, used data on pregnant women in Hlabisa, a rural area in KwaZulu-Natal. The options compared were: no PMTCT (0), provision of Zidovudine with current infrastructure (1), and provision of Zidovudine with enhanced infrastructure (2). The results of the study were that relative to no PMTCT (0), provision of Zidovudine with current infrastructure (1) reduced HIV infections by 15% at a total cost of US\$574,825, while provision of Zidovudine with enhanced infrastructure (2) reduced infections by 47% at a total cost of US\$764,901. Wilkinson *et al.*'s (1998) study was based on trials conducted in developed countries which had been deemed inappropriate to conditions in the developing world. Soderlund *et al.* (1999) supplemented the evidence on the CE of PMTCT by comparing several short-term options such as ARV with breastfeeding and ARV without breastfeeding to provide PMTCT; and found that options with formula feeding were the most cost-effective.

While Soderlund *et al.* (1999) compared the CE of such options on hypothetical cohorts of 20,000 pregnancies; Wilkinson *et al.* (2000) modelled the CE of a short course of Zidovudine with formula milk for four months nationwide (1), comparing this option with no PMTCT (0). The study found that without PMTCT (0), 63,397 infections would occur annually. They further estimated that averting these infections with PMTCT (1) would cost R155.9 million (about US\$17 million).

A related study by Wood *et al.* (2000) compared different scenarios of PMTCT rollout nationwide, notably no PMTCT (0), 25% of PMTCT coverage (1), 75% coverage (3) and 100% PMTCT coverage (4). According to the study results, 110,000 HIV-positive births could be prevented by a short course of antiretroviral therapy. Table 4.7 summarises CE studies of PMTCT, which focused on more diverse issues after 2000.

Table 4:7 Summary of CE studies of PMTCT interventions in South Africa

Biomedical prevention intervention	Evolution of CE studies	Methodological features			Citation, analysis number and study number ¹¹
	Study area Options	Methods	Results	Recommendation	
PMTCT	South Africa No provision PMTCT (0) Provision of PMTCT (1)	Used calculations based on the costs and health benefits employing data on the South African population from a variety of sources	Costs of treating opportunistic infections would be greater than the costs of PMTCT	Recommended PMTCT or else the government would be misusing tax payers' money.	Skordis & Nattrass (2002) (22) (20)
	No PMTCT (0), PMTCT (1)	Used the projections of the Actuarial Society of South Africa model	No separate results as the study was part of a larger study	No conclusion as the study focused mainly on costs.	Geffen <i>et al.</i> (2003) (23)
PMTCT	South Africa (0) current screening in early pregnancy at week 20, (0) and early and late pregnancy screening (week 20, and 34 or 36) (1)	Hypothetical population of 100 000 women modelled on different PMTC options	Rescreening was more cost-effective where ART was available and remained cost-effective where it was not	Rescreening was recommended.	Soorapath <i>et al.</i> (2006) (24) (21)

These analyses focused on the costs of government's refusal to provide PMTCT and how many times and when HIV screening of pregnant women on PMTCT should be done to maximise the benefits of the intervention. In this respect, Skordis and Nattrass (2002) estimated that the cost of infant infections in terms of social assistance and treatment of opportunistic infections, which the government was compelled to pay for by law, outweighed the cost of PMTCT. They argued that the

¹¹ The first and second number of each study in the 5th column of the Table denotes the study comparison and the study count respectively. There are more comparisons than studies because some studies made comparisons which spanned different categories of interventions. The study comparisons and count are numbered consecutively from the first Table in section 4.1.1.

government's refusal to implement PMTCT meant paying (for the treatment of opportunistic infections and social assistance) to waste lives (Skordis & Nattrass, 2002:1). Their arguments were confirmed to some extent by Geffen *et al.* (2003), who estimated that significant costs of treating opportunistic infections would be saved if PMTCT was run at coverage of 90% alongside other major HIV/AIDS interventions.

While the CE of PMTCT in the above studies was based on once-off screening for HIV/AIDS at week 20 of pregnancy, Soorapath *et al.* (2006) argued that HIV infections that could not be detected at week 20 could be detected later in the pregnancy. This led them to compare the CE of screening once in week 20 of pregnancy (0) and screening twice, in week 20 of pregnancy and later during the pregnancy (1). The study found that rescreening was cost-effective whether or not HAART was sufficiently available. Table 4.8 shows CE studies of other biomedical interventions, notably condom usage, circumcision, and antiretroviral drugs prophylaxis conducted before 2010.

Table 4:8 Summary of CE studies of other biomedical prevention interventions in South Africa conducted before 2010

Other biomedical prevention interventions	Evolution of CE studies	Methodological features			Citation, analysis number and study number ¹²
	Study area Options compared	Methods	Results	Recommendation	
Condom usage	Mpumalanga Male condom only among casual sex workers (0), Male and female condom (1)	Population of 1 000 casual sex workers Hypothetical mathematical simulation model	The programme would generate net savings of US\$5,421 if prevalence is 25%	Female condom programme targeted at casual sex workers is highly cost effective and can save public sector money.	Marseille <i>et al.</i> (2001) (25), (22)
Condom usage	South Africa and Brazil: No nitrile female condom to current use of male condom(0), Nitrile condom use to current use of condom (1)	Modelling the population of South Africa aged 15-49 sexually active in the preceding year	Countrywide distribution of female condoms	Concluded that female nitrile female condom can be cost effective.	Dowdy <i>et al.</i> (2006) (26), (23)
STD treatments	Hillbrow, Johannesburg Syndromic management with no periodic presumptive treatment (PPT) (0), (syndromic management with PPT1)	Used hypothetical cohort and a mathematical model	ICER of PPT was US\$31 per DALY averted. Initiating PPT at 15% prevalence level would have improved CE by 35%	Interventions targeted at HIV prevalence are cost effective at all HIV stages. PPT could improve the CE of targeted STI interventions.	Vickerman <i>et al.</i> (2006 a) (27), (24)
Circumcision	Orange Farm: No circumcision (0), Circumcision (1)	Used a hypothetical population of 1 000 modelled using a spread sheet	The ICER was US\$181 per infection averted with an HIV prevalence of 25% while it would be US\$551 per infection averted in areas with prevalence rate of 8.4%	Male circumcision is cost effective in high and moderate prevalence contexts even with low coverage.	Kahn <i>et al.</i> (2006) (28), (25)
Antiretroviral drugs prophylaxis	Area : South Africa No post-exposure prophylaxis to women and girls after rape (0), post-exposure prophylaxis to women and girl after rape (1)	A spread sheet based model was used to make estimations	The savings would be US\$31,630 per case averted assuming universal access to HAART and US\$331 saving per life year gained	The provision of pos-t exposure prophylaxis is cost saving and in cases of uncertainty it remains cost-effective.	Christofides <i>et al.</i> (2006) (29), (26)

¹² The first and second number of each study in the 5th column of the Table denotes the study comparison and the study count respectively. There are more comparisons than studies because some studies made comparisons which spanned different categories of interventions. The study comparisons and count are numbered consecutively from the first Table in section 4.1.1.

The earliest study comparing the CE of condom usage was conducted by Marseille *et al.* (2001) who compared the CE of using male condoms only (0) and using both male and female condoms (1), among casual sex workers in Mpumalanga. Marseille *et al.* (2001) found that using both male and female condoms (1) would generate a net saving of US\$5,421 at a prevalence rate of 25%. A related study by Dowdy *et al.* (2006) was conducted at international level and involved South Africa and Brazil. This study compared the CE of using male condoms only (0) and using both male condoms and nitrile female condoms (1). The results of the study showed that using both male and female condoms was more cost-effective in South Africa than it was in Brazil.

Kahn *et al.* (2006) examined the CE of circumcision. Using data from Orange Farm in Gauteng, the study compared the CE of no adult male circumcision (0) and adult male circumcision (1). It found that relative to no adult male circumcision (0), the incremental cost per infection averted by adult male circumcision (1) would be \$181 with an HIV prevalence rate of 25%. Although their study, like other studies elsewhere, showed that it was cost-effective to circumcise adult men, the intervention recommendation was made against the backdrop of a likely increase in risky behaviour among circumcised men.

The CE of treatment of other sexually transmitted diseases, which has been rather less controversial, was investigated by Vickerman *et al.* (2006). The study compared the CE of syndromic management without periodic presumptive treatment (0) and syndromic management with periodic presumptive treatment (1). It found that, relative to syndromic management without periodic presumptive treatment (0), the incremental cost per DALY averted by syndromic management with periodic presumptive treatment (1) was US\$31.

Other CE studies on biomedical prevention interventions compared the CE of providing antiretrovirals to people who are more exposed to HIV infections. In this regard, Christofides *et al.* (2006) compared the CE of not providing antiretroviral drugs prophylaxis to a person after being raped; that is, post-exposure prophylaxis

(0) and providing antiretroviral drugs prophylaxis to a person after being raped (1). The study found that the cost-saving of post-exposure prophylaxis (1) relative to no post-exposure prophylaxis (0) would be US\$31,630 per case of HIV infection averted. In 2010, CE studies of other biomedical interventions were conducted on pre-exposure prophylaxis and microbicides as shown in Table 4.9.

Table 4:9 Summary of CE studies of other biomedical prevention interventions in South Africa conducted since 2010

Other biomedical prevention interventions	Evolution of CE studies	Methodological features			Citation, analysis number and study number ¹³
	Study area Options compared	Methods	Results	Recommendation	
ARVs Prophylaxis	South Africa Pre-exposure prophylaxis (0), no pre-exposure prophylaxis (1)	Age and gender structured model of the generalized epidemic in South Africa	Pre-exposure prophylaxis targeted at age 15-35 would avert 10 to 15% of infections in this group and the cost per infection averted would be US\$12,500	To have a high relative CE impact on reducing infection in generalised epidemic Prep must use window opportunity until HAART has reached high levels.	Pretorius <i>et al.</i> (2010) (30), (27)
Microbicide	South Africa: No microbicide in the population of females aged 15-49 where male condoms are used (0), and microbicide in the population of females aged 15-49 where male condoms are used (1)	Modelling using an epidemiological model	The intervention would prevent 1,980 new infections and would save US\$6,712 if infection were treated through HAART	Microbicide is very cost-effective in a country with a generalised epidemic such as South Africa.	Verguet & Walsh (2010) (31), (28)

Pretorius *et al.* (2010) compared no provision of antiretroviral drugs to a person exposed to risks such as needle pricks, that is, no pre-exposure provision of

¹³ The first and second number of each study in the 5th column of the Table denotes the study comparison and the study count respectively. There are more comparisons than studies because some studies made comparisons which spanned different categories of interventions. The study comparisons and count are numbered consecutively from the first Table in section 4.1.1.

antiretroviral drugs (0) and pre-exposure provision of antiretroviral drugs (1). The study found that pre-exposure provision of antiretroviral drugs (1) targeted at age 15-35 years old would avert 10 to 15% of HIV infections.

Verguet & Walsh (2010) focused on the CE of using microbicides. Microbicides are chemical ointments which are applied by women prior to sexual intercourse to protect them from infection. However the effectiveness of microbicides in randomised controlled trials has been disappointing. Verguet & Walsh (2010) estimated the CE of not using microbicides (0) and the CE of using microbicides (1) comparing these results in South Africa and in the US. The comparison of the results showed that using microbicides (1) was more cost-effective in South Africa than it was in the US.

4.1.1.3 Behavioural prevention interventions

Despite behavioural HIV/AIDS prevention interventions being the earliest HIV/AIDS interventions category, the review unearthed only a few CE studies, most of which are very recent. These studies are summarised in Table 4:10.

Table 4:10 Summary of CE studies of behavioural prevention interventions in South Africa

Behavioural prevention interventions	Evolution of CE studies	Methodological features			Citation, analysis number and study number ¹⁴
	Study area Options compared	Methods	Results	Recommendation	
Mass media	No mass media (0), mass media (1)	Used survey by CASE to determine who was reached by the intervention and who was not	Large difference in knowledge, attitudes and action for exposure group relative to non-exposure group. Cost per change in knowledge, attitudes was low but no basis.	There was no basis for concluding whether the intervention was cost-effective.	Muirhead <i>et al.</i> (2001) (32), (29)
Counselling	South Africa current screening practice (0) one time screening (1) screening every 5 years (2) annual screening (3)	Hypothetical population modelled using CEPAC model	ICER US\$1,570/QALY for screening every 5 years over current practice ECER of US\$1720/QALY over current practice.	Annual screening is very cost-effective based on the finding that CER is less than GDP/capita of US\$5,400.	Walensky <i>et al.</i> (2011) (33)
VCT	South Africa No VCT (1) VCT (2)	Used the projections of the Actuarial Society of South Africa model	No separate results as the study was part of larger study.	No conclusion as the study focused mainly on costs.	Geffen <i>et al.</i> Nattrass, & Raubenheimer (2003) (35)
Structural interventions	Limpopo no microfinance with training (0), microfinance with training (1)	Used results from cluster trials which provided the intervention in 2009	The ICER was US\$711 per intimate partner violence-free year gained per woman.	The findings indicate that the trial phase was cost-effective and very cost-effective in the scale-up phase.	Jan <i>et al.</i> (2011) (34), (30)

The earliest study in the reviewed period is the study by Muirhead *et al.* (2001) which compared the CE of the 4th Soul City series. This was a multi-media

¹⁴ The first and second number of each study in the 5th column of the Table denotes the study comparison and the study count respectively. There are more comparisons than studies because some studies made comparisons which spanned different categories of interventions. The study comparisons and count are numbered consecutively from the first Table in section 4.1.1.

campaign to provide education about HIV/AIDS. In evaluating the CE of this intervention, Muirhead *et al.* (2001) compared the CE of no 4th Soul City series (0) and the 4th Soul City series (1). The cost per change in the knowledge of HIV/AIDS was estimated to be very low.

While this study was conducted in the early 2000s, the remaining studies on behavioural prevention interventions are very recent. One such study by Jan *et al.* (2011) compared the CE of no Intervention with Microfinance for AIDS and Gender Equity that is, no IMAGE (0) and IMAGE (1). Relative to no IMAGE (0), the incremental cost per intimate partner violence averted by IMAGE (1) was US\$711. Another study by Walensky *et al.* (2011) analysed VCT by comparing the CE of current screening practice (0), one time screening (1), screening every five years (3) and annual screening (4). The study found that the incremental cost per QALY gained of annual screening (4) relative to the current screening practice (0) was US\$1,570.

With regard to how these HIV/AIDS interventions' options were compared, Tables 4:1 to Table 4.10 above provided a summary of the CE comparison of each category of HIV/AIDS interventions but did not provide details on how cost and effectiveness were analysed. This is discussed in the next section.

4.1.2 Methodology of CE studies in South Africa

In analysing the cost and effectiveness of HIV/AIDS interventions, the CE studies in South Africa defined, for each of the compared interventions, the characteristics of patients, how the follow-up was done, how the cost and effectiveness were measured, and the criteria that formed the basis for the recommendation of any HIV/AIDS intervention. Table 4:11 shows that, CE analysis in South Africa complied to a considerable extent with the practice of CE analysis.

Table 4:11 Descriptive summary of the conduct of CE studies of HIV/AIDS interventions in South Africa

Activity	Methods used	Percentage of the studies (%)	Sources
Intervention design	<ul style="list-style-type: none"> -Followed up actual population of patients -Followed up hypothetical population of patients -Used CEPAC -Used Markov -Used projection models -Other models 	<ul style="list-style-type: none"> 90% of reviewed studies 10% of reviewed studies 30% of reviewed studies 30% of reviewed studies 15% of reviewed studies 25% of reviewed studies 	Compiled from the studies in Tables 4:1 to 4.10
Measurements of effectiveness and costs	<ul style="list-style-type: none"> -Sites as sources of baseline information -The literature as a source of baseline information -The perspective of analysis defined -Government perspective -Included societal perspective -Discount of costs were explicitly referred to -3% per cent discount rate was applied -Exclusive use of partial measures of health -Included at least multidimensional health measure (DALY, QALYs) -The cost were measured in international dollars 	<ul style="list-style-type: none"> 60% of reviewed studies 30% of reviewed studies 90% of all studies 90% of reviewed studies 20% of reviewed studies 70% of all studies 70% of studies reporting discount rate 20% of all studies 60% of all studies 90% of reviewed studies 	
Presentation of results and their generalisation	<ul style="list-style-type: none"> -Result reported using ICER -Generalisation by sensitivity analysis -Generalisation by changing selected variables (one-way, two-way, multi-way sensitivity analysis) -Generalisation by changing all variables 	<ul style="list-style-type: none"> 90% of reviewed studies 100% of reviewed studies 40% of all studies 20% of all studies 	
Intervention recommendation	<ul style="list-style-type: none"> -Indicated the basis for CE recommendations -Basis was the willingness to pay -The basis was affordability (portion of budget) -The basis was CER threshold by WHO 	<ul style="list-style-type: none"> 60% of reviewed studies 35% of all studies with a recommendation basis 10% of all studies with a recommendation basis 20% of all studies with a recommendation basis 	

Briefly, CE analysis consists of a systematic assessment of both the cost and effectiveness in terms of the health outcomes of alternative HIV/AIDS policy options for consideration by policy makers (Drummond *et al*, 2005:15). The options usually involve the baseline intervention or the comparator such as those noted (0) in Tables 4:1-to 4:10, with which the proposed HIV/AIDS intervention is compared. CEA considers the proposed HIV/AIDS intervention to be cost-effective (worthwhile) if the additional health benefits are worth the additional costs, reported in terms of the ratio of additional costs to additional effectiveness; this is known as the incremental CE ratio (ICER). The worthiness of the intervention is based on established ICER thresholds, on cost per unit of health benefits usually expended on related health care interventions, the portion of the budget the intervention requires, and on the cost-saving nature of the intervention (the intervention costs less than the comparator for the same effectiveness). The role of CEA in policy making is limited at the proposal stage to the ultimate decision on whether to select the proposed HIV/AIDS intervention or the comparator. This is the prerogative of the policy maker, who has to make a decision based on many considerations such as ethical issues, budgetary requirements, and political interests.

In assessing the costs and effectiveness of HIV/AIDS interventions, CE studies in South Africa followed up patients in each of the compared HIV/AIDS interventions by either observing costs and effectiveness in an actual population of patients or modelling such costs on a hypothetical population of patients. It is noted that 90% of the reviewed studies followed up a hypothetical population of patients using models which assumed the proportion of patients in HIV stages over time; these assumptions formed the basis of the measurement of costs and effectiveness. The most common models used were decision tree, CE of preventing AIDS complications (CEPAC), Markov states transition models, and population projection models. Of the modelled CE studies, 60% of the costs and effectiveness data were based mainly on baseline information from cohort sites, while the rest were based on evidence from the literature. While the estimation of costs in each of the modelled HIV/AIDS interventions used evidence on costs and effectiveness in HIV stages from the literature, some studies made estimations based on data observed at some sites (for example, Cleary *et al.*, 2004; Badri *et al.*, 2006).

Regarding the analysis of costs, the studies in South Africa took account of the fact that the cost to be included depended on the perspective of the funder. Ninety percent (90%) of CE studies of HIV/AIDS interventions in South Africa clarified the perspectives of the analysis. The government or public sector perspective was the most considered in CE studies. Of the studies reviewed, a small percentage (20%) included analysis that took account of the costs to society despite the recommendations of the panel of experts in CEA to consider such costs (Gold *et al.*, 1996). With regard to the time preference of HIV/AIDS interventions, 70% of the studies reported on discounting. Of these studies, 70% applied a discount rate of 3% as recommended by the panel of experts in CEA (Gold *et al.*, 1996). Finally, 90% of the reviewed studies reported costs in international Dollars or US\$ to allow for comparison with the results of other studies.

Measures of effectiveness ranged from output measures, to intermediate measures and final measures. Output measures consisted of condom distribution (see Marseille *et al.*, 2001 for example), while intermediate measures consisted of infections averted (see Hausler *et al.*, 2006 for example) and final measures consisted of life-years gained, QALYs gained or DALYs averted (see Bachmann *et al.*, 2006 for instance). Of the reviewed studies 20% exclusively used partial measures of effectiveness, whilst 60% used at least a multi-dimensional measure of effectiveness such as DALY or QALYs as recommended by the panel of experts in CEA (Gold *et al.*, 1996). QALYs are measures where the quality of life is applied (% of perfect health) to the total number of years in each HIV stage to give the total number of years of perfect health (QALYs) achieved by an HIV/AIDS intervention, while disability weight (% of perfect health lost) is applied to total number of years in a health state to determine the total number of perfect years lost (DALYs) in each HIV/AIDS intervention.

The results of CE studies in South Africa were generalised to the population by conducting sensitivity analysis on uncertain parameters. Of the reported results, 60% were generalised on the basis of the sensitivity of the results to changes in selected parameters such as exchange rate, whilst 40% were generalised on the basis of the sensitivity of the results to changes in all parameters.

Studies in South Africa used many criteria to recommend HIV/AIDS interventions as cost-effective to policy makers. These criteria consisted of the willingness to pay (the cost per effectiveness comparable to the cost usually paid by policy makers for other health care interventions) or CE thresholds suggested by experts. Other criteria were the extent to which an HIV/AIDS intervention was affordable or the extent to which it absorbed available budget.

Of the studies reviewed, 35% recommended HIV/AIDS interventions on the basis of the cost of related health care interventions. Wilkinson *et al.* (2000), for instance, indicated that PMTCT, which cost US\$17 per DALY averted in KZN and US\$46 per DALY averted in the Western Cape was cost-effective as the cost was in line with the cost of other HIV/AIDS interventions such as immunisation, which cost US\$25-30 and family planning, which cost US\$100-150 per DALY averted.

While 35% of the reviewed studies recommended HIV/AIDS interventions on the basis of the CE of related health care interventions, 20% of the reviewed studies recommended HIV/AIDS interventions on the basis of CE thresholds suggested by the WHO. These CE thresholds consisted of estimates of cost per life-year gained or per DALY avoided. Using life-years gained as health outcome measures, the WHO estimated that any health care intervention with CE estimates below a CE threshold of US\$100 per life-year gained (WHO, 2002) is cost-effective, while using DALY, the WHO estimated that an intervention is "cost-effective" if its cost per DALY is less than three times GDP per capita and "highly cost-effective" if its cost per DALY is less than GDP per capita (WHO, 2003).

For example, based on the WHO criteria, Geffen *et al.* (2000) indicated that PMTCT was cost-effective because the cost per life-year gained was less than US\$100. Moreover, Jan *et al.* (2011) found the cost per DALY averted of US\$7,688 in a trial intervention and US\$2,307 in a large scale-up of the trial to be cost-effective and highly cost-effective, respectively on the basis of the WHO criteria and South Africa's GDP per capita of US\$4,666 at the time.

Other studies recommended HIV/AIDS interventions on the basis of their affordability or the portion of the budget absorbed by such an intervention. Wilkinson *et al.* (2000) suggested that PMTCT would be cost-effective since it would absorb only 1% of the health budget or US\$0.49 per person living in South Africa. While a number of studies recommended HIV/AIDS interventions, it is important to note that a significant number of reviewed studies (60%) recommended these interventions as cost-effective without specifying the criteria which guided their recommendations. Such studies include Verguet & Walsh (2010), among many others.

With regard to how the results were reported, the ICER was the most common reported statistic. The ICER is calculated as the ratio of the difference in costs to the difference in effectiveness for two interventions: the HIV/AIDS intervention under analysis and the comparator. The ranges of ICERs per measure of effectiveness in reviewed studies comparing no HIV/AIDS intervention (0) and HIV/AIDS intervention (1) are reported in Table 4:12.

Table 4:12 Summary of ICERs per effectiveness measure and per type of HIV/AIDS intervention

Type of effectiveness measure	HIV/AIDS Treatment and care intervention <i>versus</i> doing nothing	Biomedical HI/AIDS intervention <i>versus</i> doing nothing	Behavioural HIV/AIDS intervention <i>versus</i> doing nothing
Per QALY Per life years gained Per DALY Per infection averted	Non-HAART care - US\$17-US\$244 US\$31-US\$78 US\$67 Source Bachmann (2006); Vickerman <i>et al.</i> (2006); (Hausler <i>et al.</i> 2006)	PMTCT - US\$47-US\$ 125 US\$1,484-3,845 Wilkinson <i>et al.</i> (2000)	Mass media -
Per QALY Per life years gained Per DALY Per infection averted	HAART US\$ 54-1701 US\$908-US\$2443 - - Source: Badri <i>et al.</i> (2006); Cleary <i>et al.</i> (2006); Bachman (2006); Boule <i>et al.</i> (2002); Badri <i>et al.</i> (2006)	Circumcision - - - -	VCT - - - -
Per QALY Per life years gained Per DALY Per infection averted	- - - -	Condom usage - - - -	Prevention of partner violence - US\$2,300-US\$7,700 - - Jan <i>et al.</i> (2011)

These results are compiled from the summary of CE studies results in Table 4.1 to 4.10. Source of data are indicated in the text. The sign “-” means that estimates are not available in the reviewed literature.

Despite the WHO (2003) recommending such comparison (2003), Table 4:12 shows that only a few of the reviewed studies compared the CE of HIV/AIDS interventions (1) relative to no HIV/AIDS interventions (0). Furthermore, the table shows that a very limited number of studies reported the ICER in terms of recommended multi-dimensional measures of effectiveness (QALYs and DALYs). This deficiency in the evidence makes it difficult to compare HIV/AIDS interventions nationally and internationally.

In terms of ICER estimates per type of HIV/AIDS intervention, Table 4:12 shows that these estimates varied considerably. For non-HAART treatment interventions, the ICER per life-year gained relative to no intervention ranged from US\$17-US\$244 (Bachmann, 2006). For the same category of HIV/AIDS interventions, the ICER per DALY avoided ranged from US\$31 to US\$78 (Vickerman *et al.*, 2006). Per infection averted, the ICER of non-HAART treatment intervention ranged from US\$67-US\$100 (Hausler *et al.*, 2006)

For HAART, the incremental cost per QALY gained ranged from US\$54 (Badri *et al.*, 2006) to US\$1,701 (Cleary *et al.*, 2006). The incremental cost per life-year gained ranged from US\$908 to US\$2,443 (Bachman, 2006; Boulle *et al.*, 2002; Badri *et al.*, 2006). For PMTCT, the incremental cost per DALY averted ranged from US\$54-57 (Wilkinson *et al.*, 2000). The incremental cost per infection averted ranged from US\$1,484 to US\$3,845 for PMTCT (Wilkinson *et al.*, 2000).

4.2 Patterns of cost effectiveness studies

Despite some CE evidence on HIV/AIDS interventions in South Africa, an analysis of the studies' patterns, in terms of their coverage of different types of HIV/AIDS interventions, the timing of the studies and the type of cost and effectiveness evidence used, shows that policy makers in South Africa were not provided with sufficient CE evidence. In terms of the type of HIV/AIDS interventions covered, the review found that the evidence was not sufficient as some HIV/AIDS interventions were understudied. In terms of timing, the evidence has been insufficient because it was not presented to policy makers at the relevant time, while in terms of the type of evidence used by the studies, most relied on observational cost and effectiveness data in pilot facilities in some provinces rather than on national, representative randomised data. Table 4:13 presents the patterns of CE evidence from studies in South Africa.

Table 4:13 Patterns of Cost-effectiveness evidence in South Africa

Interventions	Number of study and percentage	Type of intervention
Prevention	18 (51%)	N/A
Treatment and care	17 (49%)	N/A
Total	35 (100%)	N/A
Biomedical prevention interventions	14 (77%)	N/A
Behavioural prevention interventions	4 (23%)	N/A
Total	18 (100%)	N/A
Biomedical prevention (PMTCT)	7 (54%)	N/A
Other biomedical prevention	6 (46%)	N/A
HAART-based treatment and care	12 (60%)	N/A
Non-HAART-based treatment and care	5 (40%)	N/A
Per timing of study		Type of intervention
Up to 2000	4 (100%) 0 (0%)	Biomedical prevention interventions Behavioural prevention interventions
2001-2008	8 (90%) 1 (10%) 10 (85%)	Treatment with HAART intervention Biomedical prevention interventions Behavioural prevention interventions
After 2008	2 (50%) 2 (50%) 2 (15%)	Treatment with HAART intervention Biomedical prevention interventions Behavioural prevention interventions
Type of evidence		Type of intervention
Per type of evidence site		
One-site evidence	8 (89%)	N/A
Multiple-site evidence	1 (11%)	N/A
Randomness status of the data		
Random data	1 (3%)	N/A
Non-random	32 (5%)	N/A

Source: Reviewed studies in Tables 4.1 to 4.10.

As Table 4:13 shows, the patterns of the coverage of HIV/AIDS interventions are such that policy makers did not receive sufficient CE evidence on some of these interventions. Despite a fair coverage of HIV/AIDS prevention and treatment interventions by CE studies (51% *versus* 49%, respectively) over the period of review, Table 4:13 shows that the evidence was relatively insufficient for some interventions in each category. For instance, CE studies of biomedical prevention interventions represented 77% of all studies on prevention interventions, suggesting a deficiency of CE evidence on behavioural interventions.

An insufficiency of evidence is also noted for biomedical prevention interventions (condom usage, prophylaxis, microbicides, circumcision, treatment of STDs) other than PMTCT. A review of the evidence revealed that more than half of the studies (54%) in the category of biomedical prevention interventions were conducted on the CE of PMTCT. Within the treatment and care category, the evidence on the CE of HIV/AIDS care is relatively deficient when compared with the CE evidence on HAART, which accounts for 60% of the CE evidence produced for HIV/AIDS treatment and care.

Furthermore, the patterns of the timing of CE evidence in Table 4:13 indicate that policy makers in South Africa were not exposed to CE evidence at relevant times. In particular, not only was there little CE evidence on behavioural interventions, but the evidence that was available reached policy makers too late. As shown in Table 4:13, no CE studies of behavioural prevention intervention were conducted before 2000, despite such interventions dominating HIV/AIDS responses at the time. Even during the period 2001-2008, CE studies of behavioural prevention interventions remained sparse, with only one such study, representing 10% of all CE evidence on prevention interventions during this period. CE studies of behavioural interventions, such as Walensky *et al.* (2011) and Jan *et al.* (2011) who analysed the CE of VCT nationwide and the CE of combining microfinance and HIV/AIDS training in Limpopo, respectively, were conducted very recently. Despite the fact that CE studies of behavioural prevention interventions would have been useful in providing CE evidence on efficient ways of influencing risky behaviours in the early days of the epidemic, this evidence emerged when it was too late.

The limitation of the evidence in terms of the patterns of the studies' timing is also noted in studies of HAART interventions. While 85% of the CE studies of HAART took place in the period 2002-2008 when they were most needed, the decrease in the rate of HAART studies since 2008, despite the evolution of the guidelines for HAART interventions, points to the limitations of the evidence. Only two studies in the public domain, Walensky *et al.* (2011) and Granich *et al.* (2012), were conducted after 2008.

Finally, the patterns of the evidence on cost and effectiveness, which tended to be facility-specific and region-specific, resulted in policy makers receiving evidence which was not representative of the whole country even though it was useful at provincial or local level. An analysis of the cost and effectiveness evidence patterns reveals that 89% of the studies used cohort data from one site as baseline information to argue the efficiency of the intervention, sometimes at national level (see Wilkinson *et al.*, 2000 for one example). Furthermore, especially for HAART, such data were relevant to high HIV prevalence provinces such as KZN (Boulle *et al.*, 2002,) or in provinces where the cohort sites were based, notably the Western Cape (Cleary *et al.*, 2004, 2006; Badri *et al.*, 2006). Few studies combined evidence from many sites as has been the case elsewhere (Freedberg *et al.*, 2001). While the sources of data implied lack of national representation of the results, another issue was the reliability of such data, which were mainly observational rather than random. Of the reviewed studies in South Africa, the data that have been recommended in CEA, random data, were only used in 3% of the studies; Jan *et al.* (2011) is an example.

The patterns of the evidence discussed above highlight the extent to which the evidence was limited. Policy makers received insufficient evidence for some interventions, some of the evidence was provided too late and most of it was not nationally representative although the latter point is not necessarily a weakness.

4.3. Extent of most needed CE evidence

The extent of the evidence of CE studies in South Africa can also be gauged by assessing whether or not the most needed evidence has been presented to policy makers. In South Africa, policy makers have a particular need for CE evidence in order to optimise the use of resources in dealing with high levels of new infections, potential HIV virus drug resistance and HIV/AIDS and TB co-infection. An assessment of the evidence shows that it has been inadequate either in terms of the absolute quantity of studies or in relation to the evidence elsewhere, as shown in Table 4:14.

Table 4:14 Inadequacy of CE studies in South Africa

Area of need	Type of absolute inadequacy	Type of relative inadequacy
Prevention		
Change in risk behaviours	Evidence is limited on the basis of the limited number of studies comparing the CE of mass media, the CE of VCT and the CE of preventing partners violence (Muirhead <i>et al.</i> , 2001; Walensky <i>et al.</i> , (2011) and Jan <i>et al.</i> (2011)	Elsewhere, evidence is available comparing the CE of mass media, CE of couple counselling versus individual counselling, CE of provider initiated counselling versus patients initiated counselling, and CE of screening different strata of risk levels among patients (Hsu <i>et al.</i> , 2012); John <i>et al.</i> (2008); Sanders (2005)
Treating STD	The evidence is limited on the basis that only one study compared the CE of preventing HIV infections by treating STD (Vickerman <i>et al.</i> , 2006)	Further CE studies could have added to the evidence in South Africa had they been conducted , such as comparing different ways of managing specific STD
Condom usage and circumcision	No CE study on condom usage was available in the public domain while only one study (Kahn <i>et al.</i> , 2006) has been conducted on the CE of circumcision	CE comparison options by Martin <i>et al.</i> (2007); Binagwaho <i>et al.</i> (2010) and Gray <i>et al.</i> (2007) on circumcision, could have added to the evidence in South Africa had they been conducted
Intervention to deal with virus resistance	The absence of CE options of dealing with virus resistance in South Africa	The absence of CE options for dealing with virus resistance in South Africa and the presence of such evidence elsewhere (Sax <i>et al.</i> , 2005; Munakata <i>et al.</i> , 2006)
Task shifting	Only two studies examined the CE of task- shifting; one on providing ARV from home (Marseille <i>et al.</i> , 2009) and another on down referral of patients from doctor-managed hospital-based clinics to nurse-managed primary health care facilities (Long <i>et al.</i> , (2011)	The absence in South Africa of studies such as comparing the CE of integrating HIV/AIDS services with primary health care (Sweeney <i>et al.</i> , (2012) or different ways of task shifting found elsewhere (Chung <i>et al.</i> , 2008)
Dealing with HIV/AIDS and TB co-infections	The absence of CE studies on options shown to be effective.	No studies were found in South Africa or elsewhere

Despite the high prevalence of risky behaviours in South Africa which have fuelled high levels of infection, there have been few CE studies on how best to prevent new HIV infections. Table 4:14 shows only three such studies, Muirhead *et al.* (2001), Walensky *et al.* (2011) and Jan *et al.* (2011). One would not expect these three studies to provide overwhelming evidence to guide policy makers. Many other studies could have been conducted. Research conducted elsewhere, for instance, included studies comparing different methods of mass

media (Hsu *et al.*, 2012) and different methods of counselling. Studies on the CE of individual *versus* couple counselling, patient-initiated *versus* provider-initiated counselling and low risk *versus* high risk patient counselling (John *et al.*, 2008; Sanders, 2005; Long *et al.*, 2010) could have improved the evidence base in South Africa.

The lack of studies on the CE of prevention is manifest in the inadequacy of CE evidence on preventing HIV infections through the treatment of sexually transmitted infections. STDs create a favourable environment for HIV transmission, especially in countries with high HIV/AIDS prevalence (White *et al.*, 2008). There is overwhelming evidence that STDs promote HIV transmission in South Africa (Auvert, 2001; Johnson & Budlender, 2002: 10; Johnson *et al.*, 2005; Johnson, 2008). Despite the CE of treating STDs being of great importance in South Africa, only one study presented such evidence (Vickerman *et al.*, 2006). Had studies elsewhere, such as Gilson *et al.* (1996) which compared the CE of preventing STDs in two settings with different prevalence levels, Kania *et al.* (2009) which compared the CE of options to screen for HIV, Syphilis and Hepatitis, and Price *et al.*, (2006) which compared the CE of different ways of managing specific STDs such as Trichomoniasis, been conducted in South Africa, the evidence base would have increased significantly.

The evidence on the CE of prevention is inadequate when assessed from the point of view of interventions which the literature has shown to be most effective, such as circumcision (Auvert, 2005; Gray, 2007) and condom usage (Bedimo, 2002). Only one study in the public domain (Kahn *et al.*, 2006) provided CE evidence on circumcision in South Africa. CE evidence on condom usage was also provided by just one study (Marseille *et al.*, 2001) and this evidence is relatively old. The kinds of CE comparisons of circumcision found elsewhere such as Martin *et al.*, 2007 and Binagwaho *et al.*, (2010) but not in South Africa are again indicative of the inadequacy of CE evidence for HIV/AIDS interventions.

The review also revealed inadequacies in terms of the CE evidence in relation to options to prevent virus resistance. Virus resistance is an expected outcome that is likely to arise in circumstances of concurrent expanded treatment and high

risky behaviours such as in South Africa. Evidence has shown that HIV-positive people on treatment increase risky behaviours once their health status has been restored (Attia *et al.*, 2009:1400); these risky behaviours may include non-adherence to treatment. Non-adherence to treatment has been identified as a source of serious virus resistance to the therapy, which can result in increase in deaths. Consequently, CE options to deal with this issue are vital. The lack of CE options to deal with virus resistance is testimony to the paucity of the CE evidence on HIV/AIDS interventions in South Africa. CE studies on virus resistance such as those conducted in countries where HAART has been made universally available to patients (Sax *et al.*, 2005; Munakata *et al.*, 2006) are needed in South Africa.

The shortage of resources has also been a critical issue in South Africa due to the burden of HIV/AIDS and an inadequate health care system. The literature has shown that delegating some tasks normally performed by senior staff to junior staff (task-shifting) or integrating HIV/AIDS services with low cost routine health services (Ekman *et al.*, 2008) reduces costs while not compromising effectiveness (Maharaj & Cleland, 2005; Babigumira *et al.*, 2009; Callaghan *et al.*, 2010; Mdege *et al.*, 2012). In South Africa, delegating some medical tasks to community workers or delegating costly hospital HIV/AIDS services to primary health care facilities has proved beneficial (Uys & Heshner, 2009; Harling *et al.*, 2007). Despite this evidence, the CE of task-shifting has not been subjected to intense research efforts in South Africa. A review of CE studies showed that only two studies assessed the CE of task-shifting, one on providing ARVs from home (Marseille *et al.*, 2009) and another on down-referral of patients from doctor-managed hospital-based clinics to a nurse-managed primary health care facility (Long *et al.*, 2011). This evidence is not sufficient given the extent of the burden of HIV and the scarcity of resources to respond to it. The absence of studies comparing the CE of integrating HIV/AIDS services with primary health care services in South Africa, which have been conducted elsewhere (Sweeney *et al.*, 2012) indicates a lack of evidence on this issue.

Tuberculosis (TB) and HIV/AIDS co-infection is a serious health threat in South Africa (Gandhi *et al.*, 2006). High mortality rates among patients co-infected with TB and HIV/AIDS (Zwang *et al.*, 2007) arise from TB or HIV/AIDS drug

resistance. Dealing with TB and HIV co-infection is resource intensive and the lack of resources has led to complaints about the lack of HIV/AIDS and TB co-infection services (Mannak, 2009). While effective options to deal with HIV/AIDS have been identified (Abdool Karim & Lawn, 2009; Abdool Karim *et al.*, 2009), evidence on the CE of such options is not available. The absence of such studies indicates the limited CE evidence in South Africa.

4.4 Extent of contextual CE evidence

Cost-effectiveness comparisons of HIV/AIDS interventions across contexts are particularly deficient in South Africa despite the potential importance of such studies in optimising resource allocations. This optimisation of resources arises from the possibility that an intervention may not be equally effective across contexts. The effectiveness of an intervention is measured by its ability to reduce the impact of HIV/AIDS. Since this impact is generated by factors not primarily targeted by HIV/AIDS interventions and these factors prevail to a different extent and pattern across contexts, an HIV/AIDS intervention may achieve different effectiveness across contexts and hence different CE. This difference in CE presents opportunities for the optimal allocation of resources in defined epidemiological and socio-economic contexts in South Africa.

Despite these opportunities, CE studies in South Africa have not directly compared HIV/AIDS interventions across epidemiological and socio-economic contexts with a view to informing South African policy makers on resource allocation across contexts. Rather, these studies benefitted international policy makers by providing the cost and benefit of HIV/AIDS interventions across international contexts (Dowdy *et al.*, 2006; Verguet & Walsh, 2010). The studies conducted in South Africa have provided little evidence on how resources could be distributed in geographical contexts on the basis of CE evidence that arises from the interaction between HIV/AIDS interventions and these context dynamics.

One study which compared the CE of HIV/AIDS interventions across contexts in South Africa is that conducted by Verguet and Wash (2010). This study compared the CE of microbicides in South Africa and the US. The results over

one year for a hypothetical population of patients showed that the cost and effectiveness in the US and South Africa were different. Over one year, the intervention would prevent 1,908 new infections in South Africa, while it would only prevent 21 new infections in the US. In South Africa, the intervention would save US\$6,712 per infection averted, when compared with the cost of treatment (in cases where a microbicide is not used). The study showed that the cost per infection averted by microbicides would amount to US\$405,077 in the US and concluded that the intervention is cost-effective in South Africa, but not in the US.

While this study was an important contribution to the literature it aimed to inform international rather than South African policy makers. The study compared the relative benefits and costs of funding HIV/AIDS interventions in a HPC (South Africa) and a LPC (US). A related study by Dowdy *et al.* (2006) compared the CE of nitrile female condom across South Africa and Brazil. Although these countries are comparable in terms of socio-economic status and risky behaviours, the CE results were different. The study found that, over a period of three years using 1,000 hypothetical patients, expanding female condom use to 10% would avert 604 infections at US\$20,683 in Brazil, while in South Africa, 9,577 infections could be averted at US\$985 per infection averted. Again the results of the study are useful to global rather than South African policy makers.

In South Africa, Wilkinson *et al.* (2000) compared the CE of PMTCT from a perspective that is comparable with the present study. The study estimated the CE of PMTCT relative to no PMTCT in different provinces. The results of this study are presented in Table 4:15.

Table 4:15 Cost effectiveness results per province for the prevention of mother-to-child transmission (PMTCT) programme in South Africa

Provinces	Prevented HIV infections	Cost per infection averted (R)	Cost per DALY(R)
Gauteng	3,809	6,625	210
North West	2,357	6,463	205
Northern Province	1,678	9,799	310
Mpumalanga	2,507	5,918	187
Free State	2,046	6,255	198
Northern Cape	204	9,495	300
Eastern Cape	3,171	7,669	247
KwaZulu-Natal	6,769	4,232	134
Western Cape	640	11,656	369
South Africa	23,181	6,724	213

Source: Data extracted from Table 1 of Wilkinson *et al.* (2000:796).

While the study provided evidence on how the CE of PMTCT compares across South Africa's provinces, its aim was to advise policy makers on the costs and benefits of HAART nationally and per province, rather than on how resources should be distributed across these provinces on the basis of the results. Furthermore, the comparison involved only one HIV/AIDS intervention, PMTCT, and did not take into account the impact of the interaction between the HIV/AIDS intervention and the context of its implementation on the CE of that intervention over time.

Another context-related CE analysis in South Africa is a study by Vickerman *et al.* (2006). The study examined whether there should be presumptive treatment (PPT) in patients with high risk behaviour, as opposed to the usual syndromic management of STDs in low risk groups. While the study provided evidence on how best to treat STDs in contextually different groups of patients, this evidence may not be applicable to patients in different geographical contexts.

The above discussion highlights why contextual CE evidence in South Africa has been limited despite its potential importance to policy makers. Although some of this evidence related to South Africa, it was more relevant to international policy makers needing to direct funding to the countries where it would achieve the greatest benefits, given the costs. Contextual CE comparisons conducted in South Africa were also limited in that they did not aim to inform policy makers how resources should be distributed in HIV/AIDS interventions across contexts. These studies focused on one intervention and compared the CE of HIV/AIDS

interventions but did not distinguish the analysis in epidemiological contexts and socio-economic contexts.

Chapter summary

This chapter reviewed the extent of CE evidence in South Africa. It found that the evidence is limited on the basis of the distribution patterns of the studies, in terms of interventions timing over time, in terms of coverage of the most important interventions for the country and in terms of CE comparisons of HIV/AIDS interventions across geographical contexts. The next chapter examines why CEA of HIV/AIDS interventions across contexts is necessary.

Chapter 5 : Contextual analysis of cost-effectiveness of HIV/AIDS interventions

This chapter discusses the need to compare CE of HIV/AIDS interventions across epidemiological and socio-economic contexts in South Africa. Section one argues this case on the basis of increasing evidence in the literature regarding the dependence of HIV/AIDS interventions' effectiveness on contexts and the implications of such dependence for costs. Section two focuses on theoretical arguments concerning such dependence and section three discusses the empirical evidence; while section four analyses the relevance of such an approach in the South African situation.

5.1. Context-dependent effectiveness and cost

Linking CE analysis of HIV/AIDS interventions to contexts is necessary because of the likely dependence of the costs and effectiveness of such interventions on the contexts. The literature claims that the effectiveness of HIV/AIDS interventions depends on the contexts; hence the likelihood that the costs of such interventions also depend on the contexts. CE analysis in contexts is necessary because of uncertainty about the extent to which the CE of HIV/AIDS interventions compares across contexts. CE analysis in contexts becomes even more crucial in the event that such analysis results in significant differences in CE estimates across contexts. Such differences constitute opportunities for efficiency in allocating resources and since these opportunities would not be revealed without CE analysis, the conduct of the latter is necessary.

As early as 2001, studies started putting forward claims that interventions should be designed according to the context for greater effectiveness (Grassly *et al.*, 2001; Wegbreit *et al.*, 2006). For instance, Grassly *et al.* (2001: 1121) proposed that it would be worthwhile to measure the variables describing epidemiological contexts in order to use such variables to choose interventions which best suit the context. Other studies have claimed that HIV/AIDS prevention interventions are complex and made up of singular components to the extent that the most "active ingredient" needs to be identified for a

particular target group in order for the intervention to be optimally effective (Bonell & Imrie, 2001: 156).

Noting that prevalence varied across South Africa's provinces, Kleinschmidt *et al.* (2007: 1163) suggested that maps of HIV prevalence could be used to effectively focus intervention on contexts of particular need. In their report, Shisana & Simbayi (2002:15) noted that greater attention should be given to the relative effectiveness of HIV/AIDS interventions across contexts in order to improve the response to HIV/AIDS. Meyer-Rath (2007) observed that South Africa needed to set priorities. In countries such as Uganda and Thailand where responses to HIV/AIDS have been most successful, tailoring interventions to epidemic dynamics has been considered a factor of success (Wegbreit *et al.*, 2006:1124).

The much vaunted dependence of HIV/AIDS interventions' effectiveness on context in the literature implies that CEA of HIV/AIDS interventions across epidemiological and socio-economic contexts is necessary. Epidemiological and socio-economic contexts represent specific contexts with different circumstances in which the impact of HIV/AIDS in terms of new infections, AIDS cases and deaths takes place, with HIV/AIDS interventions' effectiveness consisting of the reduction of the impact. Because the extent of the reduction of the impact of HIV/AIDS depends on how the intervention interacts with the circumstances influencing the impact in each context, and because these circumstances differ across contexts, the latter become important determinants of HIV/AIDS interventions' effectiveness (Grassly *et al.*, 2001; Weigbreit *et al.*, 2006). Such dependence is a source of efficiency because the difference in effectiveness across contexts for a given cost of HIV/AIDS interventions opens up opportunities for efficient resource allocation.

While on the one hand, HIV/AIDS interventions' effectiveness depends on contexts, on the other, HIV/AIDS interventions' activities, and hence the costs of such interventions, also depend on contexts. Other studies analysing the factors influencing the costs of HIV/AIDS interventions only examined the change in costs in relation to the duration and scale of the intervention (Dandona *et al.*, 2008; Menzies *et al.*, 2012) and overlooked the effects of contexts on the cost of

interventions. The influence of contexts on the cost of interventions can be argued on the basis of the influence of the contexts on the impact of HIV/AIDS. Contexts influence the impact of HIV/AIDS in terms of severity of illness or the number of people affected. In influencing illnesses, contexts also influence the cost of interventions, at least indirectly. The contexts influence the cost of interventions because the latter earmark specific activities for specific types of impact (for example, severity and intensity). Since the contexts determine the type of impact, they also determine the type of activities of interventions and ultimately the cost of the interventions.

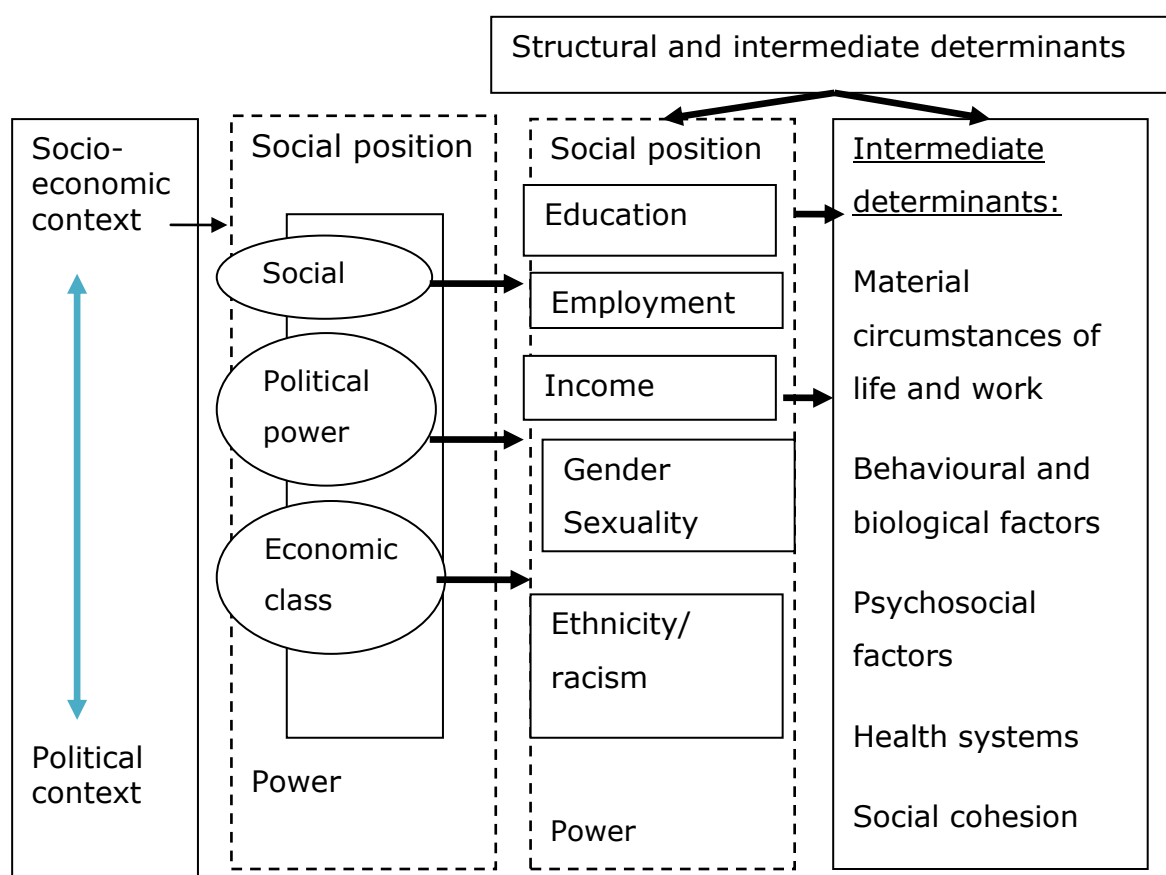
The above discussion implies that HIV/AIDS interventions' effectiveness and costs depend on epidemiological and socio-economic contexts. This suggests that HIV/AIDS interventions might achieve different incremental CE ratios (ICERs) across these contexts. Since different ICERs imply different opportunities for efficiency in allocating resources, it is necessary to conduct CE studies across epidemiological and socio-economic contexts.

5.2 Theoretical arguments

CEA across epidemiological and socio-economic contexts is necessary because the theoretical determinants of the impact of HIV/AIDS depend on the context on the one hand while on the other, the effectiveness (reduction of the impact) and the cost of interventions depends on the impact of HIV/AIDS. Like the impact of any other illness, the determinants of the impact of HIV/AIDS range from contextual factors to individual factors which cannot be expected to be the same across different contexts or even across similar contexts. These factors affect the effectiveness and cost of HIV/AIDS interventions in an uncertain manner. Consequently, not only can the patterns of the CE of HIV/AIDS interventions not be predicted across contexts, but also their extent. The insufficiency of the evidence on the pattern and extent of the CE of HIV/AIDS interventions across contexts implies a need to estimate them.

A social theory of the determinants of health status which has recently dominated the literature in explaining health status, ties the impact of illness to socio-economic factors. Figure 5:1 depicts the formulation of the theory that is

relevant to this study in that it shows the factors influencing health, which can differ from a context to another.



Source: Spanish Commission for Reducing Health Inequalities (2007)

Figure 5:1 Model of the socio-economic determinants of health outcomes

In this theory, social and economic levels are the deepest determinants of health status. Social and economic levels are characterised by income levels, education and gender relationships, and relate to health outcomes through material circumstances, psychosocial and behavioural factors, access to health and social cohesion (Valentine & Solar, 2011; Marmot & Wilkinson, 2005). The theory postulates that lower social and economic status are associated with lower income and education levels and unhealthy gender relationships. The theory has mainly been used to explain disparities in health across regions with differing income levels.

An implication of the social theory with respect to HIV/AIDS is that socio-economic contexts of lower status are associated with lower income levels to respond to HIV/AIDS, lower levels of education in general and knowledge about HIV/AIDS in particular and more exposure to risky behaviour such as injecting drugs and exchanging sex for money. A lower socio-economic position is also associated with environmental hazards, which cause stressors which in turn lead to drug addiction, alcoholism and consequently the risk of HIV/AIDS infection. In other words, the impact of HIV/AIDS in terms of new infections, AIDS cases and deaths at an individual level is on average higher in contexts with lower socio-economic status.

Models embedded in this theory have tended to focus on specific factors. Some focused on cultural factors, stating that an unfavourable HIV/AIDS cultural environment is expected in contexts with lower socio-economic status (Airhihenbuwa, 2004). Other models such as social capital theory have focused on social cohesion. Social capital theory explains that social cohesion, trust and networking help to achieve common health goals (DiClemente *et al.*, 2002). In the case of HIV/AIDS, social capital facilitates the reduction of stigma. As a result, the impact of HIV/AIDS is reduced in contexts in which greater social capital exists.

While this theoretical framework suggests that contexts with lower socio-economic status are associated with the increased impact of HIV/AIDS relative to contexts with higher socio-economic status, the question remains: to what extent is this case? The factors underlying the differences in the impact of HIV/AIDS in one pair of contexts, say an LPC and a HPC, might be different from the factors underlying the impact in another pair of an LPC and a HPC. For instance, while higher alcohol abuse might be responsible for the difference in the impact of HIV/AIDS in a pair of an LPC and a HPC, in another pair of an LPC and a HPC, gender violence might be the main factor. Even where the same factor, say gender violence, underlies the difference in the impact for the two pairs, the extent of the factor might be greater in one pair than in another.

The discussion in the paragraph above applies to pairs of different contexts, say an LPC and a HPC. Would predicting the impact across contexts be easy in a pair

of similar contexts, say an LPC and LPC? The extent of the impact of HIV/AIDS may be even more difficult to predict from one pair of similar contexts, say an LPC and LPC to another pair of an LPC and LPC because of the complex outcomes of the interaction between the contextual factors and individual factors in these two pairs of contexts. However, with modelling, this impact can be estimated.

Theories explaining individual factors in the impact of HIV/AIDS have indicated that these factors may or may not depend on the contexts in which the individual lives. Most of the individual factors influencing the impact of HIV/AIDS have been explained by psychosocial theories or theories of individual behaviour. These theories focus on how factors such as learning influence risky behaviour (Bandura, 1986; Becker, 1976). According to these theories, the impact of HIV/AIDS in a group of patients will be reduced depending on their ability and willingness to learn how to avoid risky behaviour. Other theories have concentrated on beliefs, attitudes and behaviour (Rosenstock, 1974; Fishbein & Ajzen, 1975; Ajzen, 1991). According to these theories, a person consistently behaves in relation to what they believe is right and in relation to their beliefs regarding the benefits and costs of such behaviour. The extent of the impact of HIV/AIDS would depend on the extent of such beliefs, on unsafe sex for example. The model by Fisher & Fisher (1992) and Fisher *et al.* (1994) focusing on HIV/AIDS risk behaviours and incorporating aspects of learning, attitudes and behaviour implies similar conclusions. Some of these theories include distal factors, that is, factors in society which influence a person's behaviour such as the person's perception of and compliance with social norms. The theories posit that individual behaviour interacts with social factors such that the impact of HIV/AIDS across socio-economic contexts depends on the extent and outcomes of such interactions. While these theories imply that the extent of the impact in a given context will depend on the preponderance of these factors and their interaction with contextual factors, their pattern and the extent of the impact of HIV/AIDS, the interventions' effectiveness and costs are not predictable across contexts, again implying the need to estimate such costs and effectiveness.

Economic theory can also be used to explain individual risky behaviour. The economic theory of risk behaviour can be traced to Becker (1976) who posited

that most human behaviour can be seen as rational and utility maximising. According to Becker (1976)'s theory, an individual balances the benefits and costs of any behaviour. Related to Becker's theory are theories by Levy (2002), Oster (2007), Bhattacharya *et al.* (2007), and Phillipson & Posner (1993). The most commonly used of these theories in empirical work is Philipson & Posner's (1993) theory. This theory explains that unsafe risky behaviour takes place mainly because of mutual benefits from sexual partners who each make a rational choice, given their individual expected benefits and costs of unsafe sexual behaviour. In terms of this theory, the benefit of unsafe sexual intercourse is the avoided disutility of condoms while the costs of unsafe sex are the cost of infection ranging from pecuniary costs such as treatment costs to non-pecuniary costs such as stigma and suffering.

The way in which the theory explains the dependence of the impact of HIV/AIDS on context is that the ratio of safe sex to unsafe sex is positively correlated with factors which increase the prevalence of HIV/AIDS such as location, gender, and age and not only with the individual preferences of sexual partners. In other words, the expected utility and costs which shape unsafe sex will depend on the characteristics of individuals and the characteristics of the contexts in which they live with respect to the risk of infection. As these factors influence unsafe sex, so they also influence the impact of HIV/AIDS. The complexity is however, that increased awareness of the impact might not translate into safer sex because of other factors. Individuals consider many other aspects of life in choosing safe sex and sometimes trade off poverty against the risk of infection by accepting, for example, unsafe sex for money. The link is however, complex as some people may avoid risky behaviour because of their inability to afford the costs of treatment. These arguments point to the fact that the impact of HIV/AIDS in any area may be a complex result of all these factors and the net impact of these factors can be estimated through modelling.

In contrast, most epidemiological models pay little attention to the incentives which push an individual to act. In particular, most epidemiological theories tend to ignore the fact that increased awareness about the costs and benefits of safe behaviour cause individuals to adopt safer behaviour. These models state that the level of HIV/AIDS impact would depend mainly on the risk of infections and

not on behaviour; what the literature has termed “random sorting” (Geoffard & Phillipson, 1996). Random sorting implies that people will choose partners irrespective of the information they have about the risk of infection. While the economic model postulates that higher prevalence and related consequences increase the costs of risky behaviour, which might discourage people demanding such behaviours, epidemiological models ignore such factors. Since the extent to which people perceive increased cost can vary from one context to another and the epidemiological model may work to varying degrees in different contexts, the impact of HIV/AIDS depending on the context is difficult to predict.

Whether or not these factors highlighted by psychosocial, economic and epidemiological theories influence the impact of HIV/AIDS independently of the contexts in which individuals live, the patterns of these factors and the extent to which they influence the impact of HIV/AIDS across epidemiological contexts or socio-economic contexts cannot be easily predicted. Consequently, not only does the extent to which HIV/AIDS interventions reduce the impact across a context depend on the context; it is also not easy to predict across contexts. Therefore, the effectiveness of HIV/AIDS interventions which depends on factors predominating in given socio-economic contexts needs to be estimated.

Arguments for the need to conduct CEA across socio-economic contexts can be transposed to epidemiological contexts. Contexts with lower socio-economic status may also be contexts with high prevalence status and contexts with higher socio-economic status contexts may have low prevalence. While this may be true, the need to conduct CEA of HIV/AIDS interventions across epidemiological contexts is also supported by the existence of a multitude of factors. For instance, individual level factors in a context with low socio-economic status, which are independent of the socio-economic status might create different prevalence contexts (a low prevalence context for instance) which do not comply with what is expected in a context with a lower socio-economic status. One of the reasons why prevalence contexts may not be easily distinguished is the fact that many factors may be at work to make up such a context. For instance, Hallett *et al.* (2007) note that, a decrease in risky behaviours in a given context to transform it into a low prevalence context, might be outweighed by high levels of exposure.

The need to analyse CE across epidemiological and socio-economic contexts separately is due to the fact that these contexts might be embedded in each other with independent factors determining the impact of HIV/AIDS in each area (Ferry *et al.*, 2001). This idea is illustrated in Figure 5:2.

A	B
<p>Low Socio-economic status context</p> <div>A Low HIV prevalence context</div> <div>A high HIV prevalence context</div>	<p>Low prevalence context</p> <div>A Low socio-economic status context</div> <div>A High socio-economic status context</div>
<p>High socio-economic status context</p> <div>A low HIV prevalence context</div> <div>A high HIV prevalence context</div>	<p>High prevalence area</p> <div>A low socio-economic status context</div> <div>A high socio-economic status context</div>

Source: Author.

Figure 5:2 Combinations of differences between socio-economic and epidemiological contexts

As Figure 5:2 shows, one might find two contexts with differing prevalence levels in each type of socio-economic status context (Column A of Figure 5:2) and a low socio-economic status and high socio-economic status context in each type of prevalence context (Column B of Figure 5:2).

These theoretical discussions highlight the fact that not only the patterns but the extent of the factors determining the impact of HIV/AIDS depend on epidemiological and socio-economic contexts. The discussion also highlighted that these patterns and extent may vary across similar socio-economic and

epidemiological contexts. While HIV/AIDS interventions' effectiveness depends on these factors, the complexity of the interaction between contextual factors and individual factors makes it difficult to predict the extent of costs and effectiveness across contexts. Therefore, for the sake of resource allocation across contexts, these costs and effectiveness need to be estimated.

5.3 Empirical evidence

The dependence of the cost and effectiveness of HIV/AIDS interventions on contexts is not limited to claims in the literature, but is also based on empirical evidence. The dependence of the CE of HIV/AIDS interventions on contexts stems from the dependence of the impact of HIV on contexts. The evidence reveals that most of the factors underlying the impact of HIV/AIDS prevail in a given context with patterns which are different from the patterns in another context (Kahn, 1996). The evidence also points to the fact that these factors indirectly underlie the impact (effectiveness) of HIV/AIDS interventions (Kahn, 1996). Consequently, the CE of HIV/AIDS interventions also depends on the context.

Factors underlying the impact of HIV/AIDS in a given context are empirically complex. These factors include risky behaviour, poverty, social norms and policy. In most cases, these factors are intertwined and their relationship cannot be disentangled. The prevalence of these factors in any context is diverse and the factors that dominate the influence of the impact depend on the context. This implies that even in similar contexts, factors may exert an influence on the impact to a different extent because of the complexity of the interaction between broad factors and individual-level factors.

In epidemiological contexts, empirical evidence indicates that mortality rates, infection rates, and AIDS cases are lower in an LPC than they are in a HPC. For example, Geoffard & Phillips (1996) point out that high rates of infections in a HPC are explained by proximity to the infected. Over time however, a HPC can experience fewer infections because of increased awareness of the dangers associated with the epidemic. Consequently, there might be a reduction in AIDS cases and deaths.

At an individual level, mortality and high HIV/AIDS prevalence which are typical of a HPC are expected to reduce risky behaviour in that context as predicted by economic theory. However some evidence shows that risky behaviour can increase because of despair caused by factors such as the constant loss of relatives (Caldwell, 2000). Other evidence has demonstrated that biological factors are important. For instance a context with multiple female partnerships is likely to suffer a greater burden of the epidemic than a context where such partnerships are limited. This difference may stem from the evidence that HIV infection is transmitted more efficiently in females than in males (Nicolosi *et al.*, 1994). Biological factors such as the prevalence of STDs also explain the impact of HIV/AIDS. Empirical evidence in this respect has been produced for Tanzania and Uganda. Treatment of STDs reduced HIV transmission to a greater degree in Tanzania than in Uganda because in the latter country, HIV transmission was taking place outside the core groups with high STI rates targeted by STI interventions (Korenromp, *et al.* 2005).

In socio-economic contexts, empirical evidence shows a greater impact in relatively deprived regions. In high income countries as well as low income countries, most afflicted people are from deprived and impoverished communities. For instance, 95% of all people infected with HIV/AIDS live in low income countries with only 5% in high income countries (UNAIDS, 2012). These patterns are also observed within sub-regions of these countries. For instance, sub-Saharan Africa, the poorest part of the world, is home to 68% of the world's infected adults and 90% of its infected children (Alistar & Brandeau, 2010:106). Factors such as poverty and related stressors such as intravenous drug injections have played a role in explaining differences in the impact across contexts with different socio-economic status. Poverty has been cited as leading to hopelessness and fearlessness about HIV/AIDS. Related to poverty is a lack of social support which accounts for higher infection rates in poor communities.

Despite evidence that factors such as the better health, education levels and well-being of better-off communities are at the centre of reduced HIV/AIDS impact, the complexity of the evidence lies in the fact that urban contexts in developing countries, which are better-off than rural contexts, have greater

prevalence rates than rural contexts (Shisana & Simbayi, 2002). This results from the concentration of youth in the city as a result of urbanisation, making this age group one of the driving factors of the epidemic (Adimora, 2012). Factors other than economic factors have been also found to be important. In Zambia, the proportion of female-headed households was the main determinant of infection, while fertility was negatively related to prevalence (Ojteg, 2008).

Further evidence shows that factors which are theoretically expected to contribute to the reduction of HIV/AIDS played the opposite role. According to theory, the well-educated are expected to be more knowledgeable about health and to avoid risky behaviours. However, in Zambia the HIV/AIDS rate was highest among the well-educated (Ojteg, 2008) while in Cote d'Ivoire, the well-off had more sexual partners (Cogneau & Grimm, 2006), although the impact could be offset by greater use of condoms (Snelling *et al.*, 2007). Analysing the socio-economic determinants of HIV/AIDS prevalence across nations, Zanakakis *et al.* (2007) found that lower GNP was not a determinant of prevalence, but that lower population densities and better health care systems were. Psychosociologists also predict that educated people are more likely to change risky behaviour as they acquire more information (Bandura, 1986).

Culture has been found to relate unfavourably to HIV/AIDS in low socio-economic contexts. Bowden *et al.* (2006) found that cultural factors such as misconceptions and intercommunity discrimination are important in contexts with lower socio-economic status in the US. In Africa, the subordination of women has contributed to HIV infection (Laga *et al.*, 2001). However, using religion as a proxy for culture, Tiruneh (2009) showed that in better-off southern Africa countries such as South Africa and Botswana, Christianity was unfavourable in relation to the culture in northern African countries which are predominantly Muslim. The reason given for this difference was that the Muslim rules prohibiting sexual intercourse before marriage, were stricter than those in the Christian religion. Other structural factors have been found to be at the centre of the impact of HIV/AIDS (Marshall *et al.*, 2009).

The above discussion shows that the factors which influence the impact of HIV/AIDS in any context can be distributed in a complex manner and that their

importance in a given context or across contexts is uncertain. The implication is that the impact of HIV depends on contexts in an uncertain manner, which implies that the effectiveness and cost of HIV/AIDS interventions also depends on contexts.

Given that the effectiveness of HIV/AIDS interventions is measured in terms of a reduction in the impact of HIV/AIDS, the factors influencing the impact also influence the effectiveness of HIV/AIDS interventions. The evidence shows that the factors influencing the impact of HIV/AIDS are somewhat related to the effectiveness of HIV/AIDS interventions. In Tanzania for example, the prevalence of STD was lower than in Uganda, as was the prevalence of HIV/AIDS. When treatment of STDs to prevent HIV infections was undertaken in these two countries, greater effectiveness was achieved in Tanzania (Korenromp, *et al.*, 2005).

Vickerman *et al.* (2006 b) analysed the way in which the impact of microbicide on HIV infection is affected by behavioural factors in two African settings, Cotonou, Benin and Johannesburg, South Africa, considered an LPC and a HPC, respectively. They found that the impact of the intervention was different because the two settings differed in terms of STD prevalence. Microbicide had a greater impact in Cotonou than in Johannesburg. The study also found that in Cotonou, most infections averted were among commercial sex workers while this was not the case in Johannesburg; it concluded that the context was important in influencing the outcome of microbicide. The effect of the different parameters underlying the differences in the impact of HIV/AIDS has also been documented by Ferry *et al.* (2001), who found that risk factors such as early sexual debut were important determinants of infections in urban populations with high prevalence (Ndola and Kisumu). These factors were however, less important in urban populations with low HIV prevalence (Cotonou and Yaoundé).

The dependence of the impact of HIV/AIDS on context implies that both the cost and effectiveness of HIV/AIDS interventions depend on context. This is mainly due to the fact that the costs are different in different settings but most importantly, the costs of intervention are correlated with HIV prevalence. Evidence presented by Hogan *et al.* (2005) showed that the cost of HIV/AIDS

interventions in two regions with different socio-economic characteristics were also different.

Evidence that the CE of HIV /AIDS interventions depends on the context is presented more directly in some studies. In the US, for instance, Cohen *et al.* (2004) found that the CE of HIV/AIDS interventions depended on the prevalence levels and on the cost per person reached. In particular, the study found that in a low prevalence heterosexual population, the most cost-effective interventions were those that targeted structures such as mass media and condom distribution. In contrast, the study found that targeting interventions at an individual level was more cost-effective in a high prevalence homosexual population. Earlier studies by Kahn (1996) and Holtgrave & Kelly (1996) found that HIV prevention targeting was more cost-effective.

Furthermore, a study analysing the cost and effectiveness of a set of HIV/AIDS interventions across the East African region (Afr-E) and East Asian region (Sear-D) (Hogan *et al.*, 2005) found that the cost and effectiveness of HIV/AIDS interventions considered individually or in combination with other HIV/AIDS interventions depended on the regions as shown in Table 5:1. The evidence from these regions, which differ on the basis of epidemiological status and socio-economic status, shows that the CE of HIV/AIDS interventions depends on epidemiological and socio-economic contexts.

Table 5:1 Variation in CE results across epidemiological regions

Interventions	Average cost effectiveness ratio:\$ international per DALY averted	
	Afr-E	Sear D
Individual HIV interventions		
Mass media	4	18
Peer education for sex workers	4	3
Peer education and treatment of STIs	4	3
School-based education	376-530	432-790
Voluntary counselling and testing	82	40
Prevention of mother- to- child transmission	34	310
Treatment of STIs	19-32	20-32
HAART	556-2,010	242-1,319

Source: Adapted from Hogan *et al.* (2005: 3).

The empirical evidence presented above shows that the CE of HIV/AIDS interventions depends on the context. The fact that many factors are at the centre of such dependence with a certain degree of complexity requires the estimation of the CE of HIV/AIDS interventions across contexts. The need to conduct CEA of HIV/AIDS interventions in epidemiological and socio-economic contexts is more evident for South Africa as discussed in the next section.

5.4 Relevance of contextual CE analysis to South Africa

Contextual analysis of CE in South Africa is relevant due to the paucity of CE evidence discussed in Chapter 4 and the absence of context-related policies outlined in Chapter 3. The fact that South Africa comprises distinct rural and urban contexts, and LPCs and HPCs also makes CE comparisons across contexts relevant. Such comparisons discussed earlier (section 4.4) would result in the efficient allocation of resources.

5.4.1 Epidemiological contexts

It has been claimed that the best way of responding to HIV/AIDS is to tailor the response to the epidemiological contexts of the epidemic (Grassly *et al.*, 2001; Parker & Aggleton, 2002; Walker, 2003). Such a response is difficult, however, because of the concurrent influence of the characteristics of the contexts and interventions on costs and health outcomes. In the case of an LPC and a HPC in

South Africa, these complex relationships imply that the CE of interventions across the two contexts is not obvious.

For some time, there have been proposals to consider contexts of intervention in terms of responding to HIV/AIDS (Grassly *et al.*, 2001:1121). The rationale for these proposals is that an HIV/AIDS intervention can have different success rates, depending on the prevalence context in which it is implemented. The extent to which an intervention succeeds depends on its net effect between the risk factors and its own effect on reducing the impact (Weigbreit *et al.*, 2006).

Risk factors are diverse, and range from structural, to epidemiological, environmental and cultural factors (Parker & Aggleton., 2002; Airhihenbuwa, 2004; Pronyk *et al.*, 2006; Raogupta *et al.*, 2008). Risk factors have been found to influence health theoretically and empirically through their influence on health-seeking behaviour, attitudes towards health interventions (Bandura, 1986; Becker, 1974; Geoffard & Phillipson, 1996), and their linkage with culture (Airhihenbuwa, 2004). They are consequently expected to be at the centre stage of differences, even in the presence of HIV/AIDS interventions, in new infections, sickness and deaths.

Calls to respond in epidemiological contexts appear to be very relevant for South Africa. Although the generalised HIV/AIDS epidemic in South African would seem to imply the need for a response targeting the general population (Whiteside & Smith, 2009), prevalence levels in the general population have been consistently different across the provinces (Statistics South Africa, 2010; 2011; 2013). Despite this feature of the HIV/AIDS epidemic, major HIV/AIDS interventions have failed to account for how these interventions would fare in contexts with different characteristics. In the context of limited resources to meet the demand for HIV/AIDS services, the question revolves around whether HIV/AIDS interventions could be more optimal in some contexts with specific prevalence levels, than in others. This question can only be answered through hard evidence on cost and health outcomes; hence the need to compare the CE of HIV/AIDS interventions across epidemiological contexts.

5.4.2 Socio-economic contexts

In response to the HIV/AIDS epidemic, South Africa has recently adopted universal coverage with highly active antiretroviral therapy (HAART) and has decided to start treatment earlier (at a threshold of 350 CD4 count) rather than later (at a threshold of 200 CD4 count). Although they might improve the welfare of the population, these policies will require considerable resources.

With some evidence available that the effectiveness and cost of HIV/AIDS interventions depend on contexts (Wilkinson *et al.* 2000), the on-going question is how to optimise the use of resources by allocating them according to the CE of HIV/AIDS interventions in a rural context and an urban context in South Africa. Rural and urban contexts are defined as distinct contexts because their environments, livelihoods and way of life are different.

The evidence that the impact of HIV/AIDS in a rural context and an urban context depends on the factors underlying the impact in these contexts provides a clue that the effectiveness of HIV/AIDS interventions also depends on these factors. Since HIV/AIDS interventions do not address all these factors, some of these factors' influence will persist even in the presence of HIV/AIDS interventions. The extent of such persistence is expected to be different across rural and urban contexts.

A number of factors have been identified as important determinants of the impact of HIV/AIDS in South Africa. Booysen *et al.* (2004) and Muntinta *et al.* (2011) highlighted poverty as a factor that aggravates the impact of HIV/AIDS. Using poverty related stressors, Kalitchman & Simbayi (2006) found that educational level, unemployment, discrimination, violence and crime were factors underlying the differences in the impact of HIV/AIDS across three communities: African townships, racially integrating townships and urban residential neighbourhoods, with different socio-economic status. Lower socio-economic status was positively correlated with the overall index reflecting no condom use, multiple partners, and exchange of sex for money, STI history and genital ulcers. Using logistic regression, Kleinschmidt *et al.* (2007:1164) mapped the geographic distribution of HIV/AIDS in South Africa and reported that the

proportion of residents who were Black, the proportion of women aged 20-64 years old who were unemployed, the proportion of informal households, and the proportion of 15-19 year-old persons who had not completed school were significantly associated with HIV infection.

While in general lower socio-economic status was associated with a greater impact of HIV/AIDS, some studies have shown a greater incidence in urban than in rural contexts. Kleinschmidt *et al.* (2007:1165), for instance, noted a lower incidence of HIV in a rural inland context in the Western Cape in relation to the incidence of HIV in the city of Cape Town. One study also reported that there were more sexual partners and earlier sexual debut in urban contexts than rural contexts due to the lack of parental control (Mathews, 2010).

A study by Bouare (2009) that modelled the contextual determinants of the prevalence of HIV/AIDS in South Africa found the determinants of risky behaviour to be fearlessness/low perception, poverty, hopelessness and gender dependence. The factors highlighted by Bouare (2009) seem to emphasise that the factors influencing the impact of HIV/AIDS are shaped by the contexts in which they occur. Fearlessness accords with the evidence that poor people in rural contexts are unaware of the danger of the epidemic. Pelitzer's (2009) study highlighted the factors associated with the level of knowledge about HIV/AIDS. These factors, which underlie the different impact across rural contexts, are also expected to underlie the effectiveness of HIV/AIDS interventions.

The literature on socio-economic determinants of HIV/AIDS also reveals to some extent how socio-economic status can influence the cost of HIV/AIDS interventions. Socio-economic status can influence cost because people of different socio-economic standing use health care differently in terms of intensity and patterns. While a greater rate of usage of HIV/AIDS interventions will increase the costs, the patterns of usage such as delaying usage until health status has seriously deteriorated can exacerbate costs. Since the usage rate and patterns can depend on socio-economic contexts, the costs of HIV/AIDS interventions are likely to depend on these contexts.

The contention that the performance of HIV/AIDS interventions depends on the contexts of their implementation and the stark differences in the dynamics in urban and rural contexts in South Africa (Department of Health, 2003 c), raise the question of whether the CE of HIV/AIDS interventions is the same across such contexts. If the CE of an HIV/AIDS intervention across these contexts is different, this difference could serve as an opportunity to achieve optimal resource allocation.

While optimal resource allocation can be achieved by intensifying interventions where they can attain the highest outcomes given the cost, this has not been routine policy in South Africa. To inform such policy, a comparison of the CE in socio-economic contexts is necessary.

Chapter summary

In conclusion, this chapter has argued the case for CEA of HIV/AIDS interventions across socio-economic and epidemiological contexts in South Africa, which consists of geographical comparisons of these contexts. This is based on the dependence of the effectiveness and cost of HIV/AIDS interventions on contexts, on theoretical and empirical support for the notion of such dependence and on the relevance of contextual analysis of the CE of HIV/AIDS interventions for South Africa. The next chapter examines how such CE analysis is conducted.

Chapter 6 : General methodology

This chapter describes the general methodology used in this study and discusses specific details of the methodology used in the subsequent analysis chapters. Patients in HIV/AIDS interventions are followed up over time using Markov modelling and the ASSA2008 AIDS model or Spectrum Policy Modelling System projections. Cost and effectiveness are estimated and the effect of the interaction between the contexts and HIV/AIDS interventions on the cost and effectiveness of these interventions is taken into account by using context-specific data and by incorporating context-specific assumptions in these models. Section one describes the design of the study, section two discusses the Markov states transition model, section three presents population projection models and section four explains data collection, while section five deals with data analysis.

6.1 Study design

For each HIV/AIDS intervention in the following contexts: a low HIV prevalence context (LPC), a high HIV prevalence context (HPC), a rural context and an urban context, a follow-up of patients is done and CE is estimated. The CE of a given HIV/AIDS intervention in one context is then compared with its own CE in another context. This comparison is done for voluntary counselling and testing (VCT), sexually transmitted infections (STD), prevention of mother-to-child transmission (PMTCT) and highly active antiretroviral (HAART) for adults and HAART FOR CHILDREN. An LPC and a HPC are termed epidemiological contexts while a rural context and an urban context are termed socio-economic contexts.

The design distinguishes different types of follow-up. In one type of follow-up, the same size patient cohort starts in the same HIV/AIDS state across contexts and this size changes as a result of death only. In another type, different sizes of patient cohorts start in different HIV/AIDS states across contexts and these sizes change over time because of migration, new births and deaths.

It is assumed that the distribution of patients in HIV/AIDS states over time depends on the interaction between HIV/AIDS interventions and the contexts in which such interventions are implemented. In the follow-up, estimates are made of costs, effectiveness and the CE of HIV/AIDS interventions in each context over a specified time horizon of HIV/AIDS interventions. The study uses two types of time horizons, the lifetime horizon of the interventions in which an evaluation of cost and effectiveness stops when all members of a cohort of patients in that intervention die and a specific time horizon in which the evaluation of cost and effectiveness stops at a specific date while some patients are still alive.

With regard to the scope of the study, CE comparisons are only done within epidemiological contexts or socio-economic contexts. In other words, the CE of a given HIV/AIDS intervention in an LPC is only compared with its own CE in a HPC for epidemiological contexts and the CE of a given HIV/AIDS intervention in a rural context is compared with its own CE in an urban context for socio-economic contexts. Therefore, the CE of a given HIV intervention is compared across two contexts at a time. The study acknowledges other contextual comparisons of HIV/AIDS such as the comparison of the CE of a given intervention in an LPC and in a rural context. These comparisons are not considered and are referred to future research due to space and time constraints. Furthermore, the study does not attempt to identify the specific factors influencing cost-effectiveness in the contexts considered or focus on a particular group of patients such as males and females.

Two types of comparisons are considered in this study. The first compares the average CE ratio (ACER) of intervening with a given HIV/AIDS intervention in one context relative to intervening with the same intervention in another context. The second is a comparison of the incremental CE ratio (ICER) of a given intervention relative to USUAL CARE (care in the case of the absence of an HIV/AIDS-specific intervention) in one context with the ICER of the same intervention relative to USUAL CARE in another context. In both types of comparison, the CE of an HIV/AIDS intervention in one context is compared with its own CE in another context using ACER and ICER as a comparison statistic. In the second type of comparison, the methodology distinguishes a situation in

which the size of the cohort of patients is the same and starts in the same HIV/AIDS state in either context, or a situation in which the size of the cohort of patients is different and this cohort of patients starts in different HIV/AIDS states.

The effectiveness of an HIV/AIDS intervention in terms of improved health status is estimated using a one-dimensional measure of effectiveness such as survival, deaths averted and life-years gained, and a multidimensional measure of effectiveness which simultaneously takes survival and the quality of life in that survival (QALYs) into account. QALYs are obtained by multiplying the percentage of perfect health in a given health state (say AIDS state) by the time (in years) spent in that state, hence providing perfect years produced by an intervention.

Briefly, the design of the study is such that CE comparisons are conducted from different points of view. This is achieved by including CE comparisons of HIV/AIDS interventions with same and different sizes of cohorts of patients, with and without USUAL CARE, with and without multidimensional measures of effectiveness, and with and without lifetime horizon. These multiple points of view are considered in one of the two modelling approaches, Markov modelling using cohort simulation and epidemiological modelling using the ASSA2008 AIDS model and SPMS.

6.2 Markov model

This section discusses the Markov model. It briefly discusses the theoretical aspects of the model and its empirical application, and shows how the model is applied in this study.

6.2.1 Theory and empirical application

A Markov model is used when the patients across the two contexts are assumed to be of the same size and start in the same HIV/AIDS state. A Markov model tracks a hypothetical cohort of patients in successive periods (cycles) of equal intervals over the time horizon of an HIV/AIDS intervention (Sonnenberg & Beck, 1993). In each period in the Markov model, patients are in mutually

exclusive HIV/AIDS states, “non-infected”, “infected”, “AIDS” and “deaths” chosen in terms of their influence on health status and costs. Belonging to a mutually exclusive HIV/AIDS state means that a patient cannot be in two HIV/AIDS states in one period.

The Markov model shows the distribution of a cohort of patients in HIV/AIDS states in short and successive periods of the interventions’ time horizon. The model determines the costs/health outcomes of an HIV/AIDS state by applying the HIV/AIDS state’s cost/ health outcomes to the number of patients in that HIV state. The numbers of patients in each HIV/AIDS state are obtained by means of the proportion of patients, called transition probabilities, who usually fall into that state from other HIV/AIDS states when a cohort of patients is followed up. The costs and health outcomes of any one period of the successive periods is obtained by summing over costs/health outcomes of HIV/AIDS states in that period. The costs/health outcomes of the model over the term of analysis are obtained by summing over cost/health outcomes of successive periods.

Technically the Markov model tracks patients in HIV/AIDS states in successive periods of the time horizon for the analysis by associating a transition probabilities matrix with each period. The transition probabilities matrix in the current period shows the proportions of patients in HIV/AIDS states who have transited to these states from other HIV/AIDS states in the previous period. Table 6:1 shows an example of the transition probabilities matrix for a current period.

Table 6:1 Transition probability matrix for a typical current period in Markov modelling

Transition from previous period	Transition to current period			
		State 1	State 2	State 3
	State 1	P11	P12	P13
	State 2	P21	P22	P23
	State 3	0	0	1
		P11+P21	P12+P22	P13+P23+1

Source: Author.

In Table 6:1, the second column from the left shows HIV/AIDS states in the previous period, the alive states (State 1 and State 2) and the dead states (State 3). The second row from the top of the table shows HIV/AIDS states in the current period. Cell P11 shows for instance, the proportion of patients from State 1 in the previous period who remain in State 1 in the current period. Cell P12 shows the proportion of patients from State 1 in the previous period that move to State 2 in the current period. The other cells in the table are defined similarly. The number of patients in each HIV/AIDS state of the current period is obtained by applying a specific size of a cohort of hypothetical patients in HIV states in the previous period to the proportions (transition probabilities) in Table 6:1.

To get the proportion of patients in HIV/AIDS states in the next period, the proportion of the cohort in HIV/AIDS states in the current period ($P_{11}+P_{21}$, $P_{12}+P_{22}$, $P_{13}+P_{23}+1$) are now in State 1, State 2 and State 3, respectively of the second column of the transition probability matrix of the next period. In this period, they are distributed in HIV/AIDS states according to the transition probabilities matrix of that period. Since only patients in the alive states transit to other states, the proportion of patients in the dead states (State 3) transit only to State 3 (indeed, they remain in State 3 and no transition takes place); over time the size of the remaining cohort to apply to the successive transition probability matrix shrinks. When almost all patients are dead no further transition is possible; the lifetime horizon of Markov modelling is reached. In this case, a hypothetical cohort of patients is applied to the model to obtain the different number of patients in HIV/AIDS states in successive periods. The cost and effectiveness evidence in HIV/AIDS states is then applied to these patients. The total cost and effectiveness of the model are then summed up. It should be noted that the comparison of the CE of two interventions implies running two Markov models.

A number of states transition models have been used to analyse the impact and cost of HIV/AIDS interventions. One of the most commonly used models is the CE of preventing AIDS complications (CEPAC) model. The Markov model is another states transition model which is appropriate in CE analysis of HIV/AIDS

interventions as it tracks the movement of patients back and forth in HIV/AIDS states, which is characteristic of HIV disease. The Markov states transition model has been recommended for diseases of this nature (Sonnenberg & Beck, 1993; Briggs & Sculpher, 1998) and has been extensively applied to analyse the consequences of HIV/AIDS both in high-income countries (Chancellor *et al.*, 1997; Freedberg *et al.*, 2001;) and low-income ones (Goldie *et al.*, 2006; Walensky *et al.*, 2008; Badri *et al.*, 2006; Cleary *et al.*, 2006).

6.2.2 Markov modeling and this study

In epidemiological contexts, this study uses one pair of Markov models for each HIV/AIDS intervention. One Markov model is constructed for an LPC and another for a HPC. A HPC includes the Eastern Cape, Free State, Gauteng, KZN and North West; while an LPC includes the provinces of Limpopo, Mpumalanga, Northern Cape and the Western Cape. A HPC has had an antenatal prevalence rate above 25%, while an LPC has had a rate below 25%. South Africa as a whole is already a HPC on the basis that it is a generalised epidemic country with an HIV/AIDS prevalence rate above 5% in the general population (UNAIDS 2010; UNAIDS/WHO, 2009). However, this study classified provinces as HPC and LPC in order to capture the effects on outcomes and costs of HIV/AIDS interventions of the differentiated epidemic which has characterised the country.

In each model, the movement of patients in HIV/AIDS states over time is first tracked using the transition probability matrix of the first three-month period determined by collecting related evidence from the literature about the proportion of patients who usually transit from a given state to another (see Section 6.4). Second, the movements of patients in HIV/AIDS states in subsequent three-month periods are tracked by making assumptions about such movements on the basis of the evidence of projection models in relation to trends in the epidemic.

In socio-economic contexts, two pairs of Markov models are constructed for each intervention. One pair consists of a model of an HIV/AIDS intervention for the rural context and a model for the same HIV/AIDS intervention in the urban context. In the absence of an HIV/AIDS intervention, patients use USUAL

CARE¹⁵. Therefore, another pair consists of a Markov model for USUAL CARE in the rural context and a Markov model for USUAL CARE in the urban context for patients who would have used that intervention. The process of tracking patients in various HIV/AIDS states over time is the same as in epidemiological contexts for the first three-month period and in subsequent periods.

In either context, it is assumed that all members of the cohort of patients start in the “non-infected” states for prevention interventions; while for HAART interventions, it is assumed that patients start in the “AIDS” state. The same size cohort of patients is also assumed in each context. The interaction between the context and the intervention is captured by basing the progression of patients in HIV/AIDS states over time in each context on the context-specific projections by epidemiological models which take such interactions into account (see Section 6.3).

In either context, the Markov model tracks (or simulates in the terminology of Markov modelling) a hypothetical cohort of patients in different HIV/AIDS states over successive three-month intervals, in line with previous studies conducted in South Africa (Cleary *et al.*, 2006) until everyone in the cohort is dead. The cohort is assumed to be similar to the population of patients who would have been using HIV/AIDS interventions since 2007. The year 2007 is chosen as the starting point of simulation because it is the year which marked the South African Government’s serious commitment to tackle the HIV epidemic (Meldrum, 2006). This study aims to advise South African policy makers on the economic implications of such a commitment.

¹⁵ It is important to note that USUAL CARE is no longer an option in the sector of HIV/AIDS interventions. However to capture the full benefit and costs of HIV/AIDS interventions in a context, the USUAL CARE and related costs had to be accounted for to provide a realistic assessment of the benefits and cost of an HIV/AIDS intervention in a context.

6.3 Epidemiological projection models

In a situation when the cohorts of patients across contexts are assumed to be of different sizes and start in different HIV/AIDS states, epidemiological projections in relevant contexts are used to estimate cost-effectiveness. The ASSA2008 AIDS model is used in epidemiological contexts, while SPMS is used in socio-economic contexts.

6.3.1 ASSA2008 AIDS models

The ASSA2008 AIDS model is used to make annual projections of patients using an HIV/AIDS intervention and health outcomes over the period 2007-2020 in epidemiological contexts, namely an LPC and a HPC as explained above. These numbers of patients are used as the basis for estimating the annual costs of that HIV/AIDS intervention by applying the annual cost per patient.

The ASSA2008 AIDS model is an updated version of the AIDS Models of the Actuarial Society of South Africa (ASSA). The first AIDS model was ASSA500. Subsequent improvements on the model resulted in ASSA600, ASSA2000, ASSA2003 and ASSA2008. In 2002, the year in which the ASSA2000 model was released, the AIDS Committee decided to name the models after the year of antenatal prevalence data used to construct the model. This means that ASSA2000, ASSA2003, and ASSA2008 were constructed based on antenatal prevalence data for 2000, 2003 and 2008.

ASSA2008 is an improvement on ASSA2003. The construction of ASSA2003 was founded on the assumption that HIV spreads *via* heterosexual encounters. The modelling distinguished the variables PRO, STD, RSK, and NOT; each capturing a different level of risk of infection. The PRO variable represented the group of people with the highest risk of infection. This group consisted of sex workers. The STD was a variable for the group of people with the next highest risk of infection and was made up of frequent carriers of other STDs. The third variable, RSK, referred to the group of people with the next highest risk of infection. This group was made up of people at risk of infection such as the youth, but not usually carriers of STDs. The variable representing the group with the least risk

of infection, NOT, captured data for the group of people not at risk. The model also took account of the differences in the spread of HIV across age, and the gender composition of these risk groups. The model used data on sexual behaviour, the probability of infection, the progression of HIV, the effect of major interventions, census data (1970, 1996 and 2001), fertility rates, the 1998 demographic and 2001 health surveys, international migration data, non-AIDS mortality data and 2008 antenatal survey data in South Africa in different epidemiological contexts considered in this study as LPC and HPC to formulate such projections. The ASSA2008 improved on the projections of its predecessors in that it took account of increased condom usage, treatment with HAART, increases in survival rates among untreated HIV/AIDS patients and a lower incidence of MTCT than had been previously modelled.

The annual cost of an HIV/AIDS intervention over the period 2007-2020 is calculated on the basis of annual projections of patients using the intervention. Where an HIV/AIDS intervention is absent, it is assumed that patients in an LPC or a HPC use USUAL CARE. Therefore, the same annual projections of the number of patients are also used to estimate the annual costs of USUAL CARE over the period 2007-2020. ASSA2008 AIDS model projections are expected to depict the effect of the interaction between an HIV/AIDS intervention and the LPC or HPC on the CE of that HIV/AIDS intervention.

6.3.2 Spectrum Policy Modeling System (SPMS)

The SPMS is used to make projections of the annual number of patients using an HIV/AIDS intervention over the period 2007-2020 in socio-economic contexts, notably the rural context and the urban context. The SPMS is a modular programme designed to assist policy makers with current and future information on the impact of HIV/AIDS, the effectiveness of HIV/AIDS interventions and resource requirements for planning purposes. It does this by allowing the interaction between a demographic projection module, an AIDS impact module and an HIV/AIDS intervention module. The SPMS is updated every two years to capture changes in the HIV/AIDS sector (Stover *et al.*, 2009).

The SPMS has been extensively used to inform policy-making at national (Rehle & Shisana, 2003; Wood *et al.*, 2000) and sub-national levels (Mekonnen *et al.*, 2002). One of the model's most recent applications was the estimation of the impact of expanded access to antiretroviral therapy in 10 sub-Saharan African countries, including South Africa (Anema *et al.*, 2011).

To make annual projections in a rural and an urban context, SPMS requires context-specific data on demographic and HIV epidemic and HIV/AIDS interventions parameters. Demographic inputs, notably the population per age and gender for the base year (1981), are collected from the United Nations Population Division. This year is chosen as the base year for the demographic projection due to the recommendation of the model builders to start the projection two years before the first AIDS case in the country; AIDS was first observed in South Africa in 1983 (Abdool Karim *et al.*, 2010:39).

Assumptions are made about life expectancy at birth and international migration over time. Life expectancy is assumed to be higher among females than males (Statistics South Africa, 2010), but no differences are assumed regarding patterns of life expectancy across rural and urban contexts over time, given the absence of evidence in this regard. The default UN Population Division's international migration variable provides country-level international migration data and was adjusted to include rural-urban migration.

With regard to the age distribution of fertility, that is, how age groups share the number of births over time, it is assumed that there are more births among young females in the urban context than in the rural context, given the tendency of younger women to move to an urban context. The total fertility rate in each area - the average number of children born to a woman in her lifetime - is set at South Africa's total fertility rate as reported in the literature (UN Population Division, 2011) due to the absence of such data in each context.

The impact of AIDS has not been routinely reported in a rural context and an urban context in South Africa, and thus also had to be modelled. Shisana & Simbayi (2002) found that HIV/AIDS prevalence was higher in an urban context than a rural one. In this study, the urban context comprised urban informal

(townships) and urban formal (metropolitan) areas, while the rural context was made up of tribal areas and farm areas.

The present study combined urban informal and urban formal areas to comprise an urban context, and tribal and farm areas to comprise a rural context, recalculated the prevalence of HIV/AIDS in urban and rural contexts based on the sample weights in each sub-area and assumed greater HIV/AIDS prevalence in an urban context up to 2010 (Shisana & Simbayi, 2002; HSRC/MRC/CADRE 2005; HSRC/MRC/CADRE, 2009). After 2010, it is assumed that the difference in the prevalence rate between rural and urban contexts decreased to converge by 2020, given evidence of the recent increase in the infection rate in rural contexts and a decrease in infection in the urban areas (Stover, 2009).

For the purposes of estimating the annual impact of HIV/AIDS in each context with the SPMS, annual HIV/AIDS prevalence is incorporated. The available evidence on HIV prevalence in rural and urban contexts is incorporated in the Estimation and Projection Package (EPP). The EPP has been used for the same purpose in other studies in South Africa (see, for example, Rehle & Shisana, 2003). The prevalence rate assumptions beyond 2010 were directly incorporated in the SPMS.

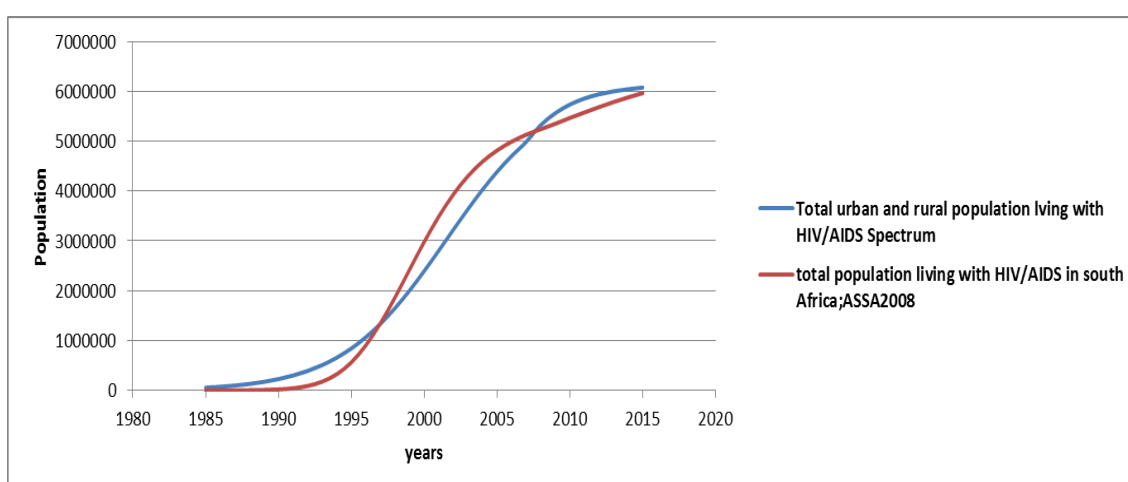
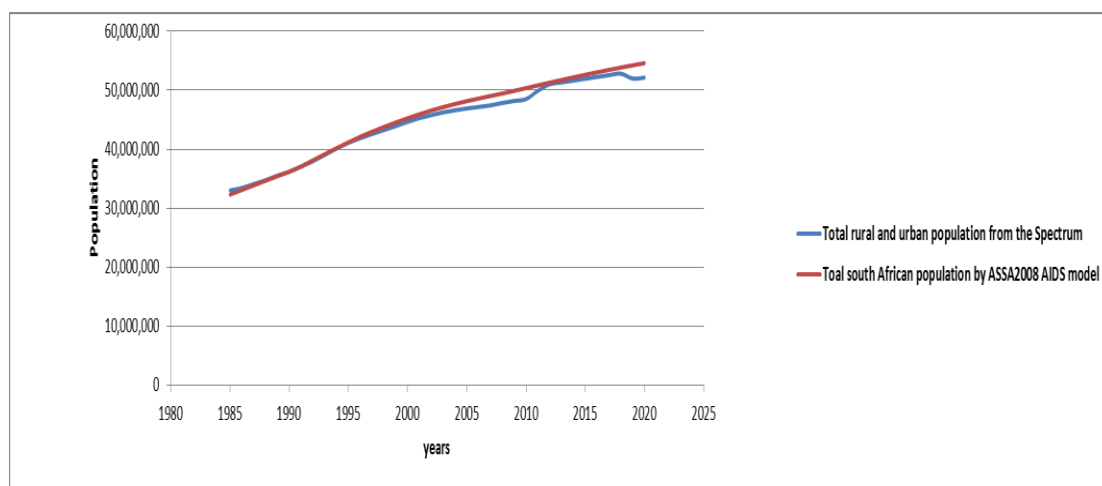
The next step in the projection of CE is to incorporate the effectiveness data for HIV/AIDS interventions. For PMTCT, it is assumed that in the absence of PMTCT the infection rate would be 30%, with a range of 25-40% among breastfeeding communities following evidence in this regard (Shaffer *et al.*, 1999). In line with recent evidence on the effectiveness of PMTCT, the infection rate with PMTCT is assumed to be 3.5% (Leach-Lemens, 2011). The study assumes that the median time from infection to AIDS death is 10.5 years for adults. The median time from eligibility for treatment (at CD4 count 350) to death is assumed to be 7.9 years for adults. The annual survival rate on antiretroviral drugs is assumed to be 90% for adults and 85% for children (UNAIDS, 2009). Table 6:2 provides a summary of key demographic and epidemiological parameters used in the projections, and Figure 6:1 compares the study's modelled data with other data.

Calibration is done to establish how these assumptions' results compare with other projections. These are presented below. The main input parameters in Table 6:2 and projections in Figure 6:1 compare favourably with other sources.

Table 6:2 Key parameters in a rural context and an urban context

Rural areas		
Baseline parameter	Base-case Value	Source
Total population in 1981	14,500,000	UN Population Division
Baseline total fertility rate	4.74	UN Population Division
Baseline life expectancy at birth in 1981		
Male	55.1	UN Population Division
Female	61.7	UN Population Division
Perinatal transmission among breastfeeding women	10%	UNAIDS(2009)
Median time from infection to death (no intervention)	10.5 years old	UNAIDS (2009)
HIV prevalence rate (general population)	8.3%	(Shisana & Simbayi,2002)
Net migration	9776	Statistics South Africa (2010)
Urban areas		
Total population in 1981	15,200,000	UN Population Division
Baseline total fertility rate	4.74	UN Population Division
Baseline life expectancy at birth in 1981		
Male	55.1	UN Population Division
Female	61.7	UN Population Division
Perinatal transmission among breastfeeding women	08%	UN Population Division
Median time from infection to death (no intervention)	8 years	UNAIDS(2009)
HIV prevalence rate(general population)	13.3%	UNAIDS (2009)
Net migration	11283	(Shisana & Simbayi,2002), Statistics South Africa (2010)

Notes: Data are produced at a national level and then adjusted based on infection trends in rural and urban areas.



Source: ASSA (2011), Stover (2011).

Figure 6:1 Comparison of modelled data with population data and prevalence data

6.4 Data collection

This section explains how data are collected for the Markov models and epidemiological projection models.

6.4.1 Data collection for Markov models

Transition probabilities for the first three-month period are collected from the literature in relevant epidemiological or socio-economic contexts. In subsequent periods, transition probability data are generated based on trends suggested by projection models in each context. In epidemiological contexts, such data are based on mortality and infection rates over time in an LPC and a HPC as suggested by the ASSA2008 AIDS model. In socio-economic contexts, they are

based on infections and mortality rate over time as suggested by the SPMS which projects the impact of interventions in rural and urban contexts. The average infections and mortality rates every year are transformed in a 3-month transition probability.

Effectiveness data collected consist of utility weights data. Utility weights equivalent to quality of life from South African studies (Jelsma *et al.*, 2005; Louwagie *et al.*, 2007; O’Keefe & Wood, 1996) are used. Using community responses about their quality of life in HIV/AIDS stages, these studies transformed data into utility weights employing empirical predictions based on expected utility methods that yielded these predictions using community responses in high income countries (Euroqol Group, 1990).

The costs are collected in the relevant literature. Cost data from a perspective other than the government’s are adjusted to reflect the latter perspective, since the South African Government is the main funder of HIV/AIDS interventions. The study includes the societal perspective to account for the full costs of HIV/AIDS interventions by adding patient transport costs and waiting time. The US Panel of Experts has recommended that the societal perspective be taken into account in CE analysis (Gold *et al.*, 1996). All costs and health outcomes are discounted at 3% in the base-case analysis taking the beginning of 2007 as time zero. Real costs are used, with 2007 as the base year. Data collected in the form of rates are transformed into transition probabilities using the formula $1 - e^{-rt}$ suggested in the literature (Sonnenberg & Beck, 1993:30).

6.4.2 Data collection for projection models

In epidemiological contexts, the annual cost per patient is collected in the South African literature in relevant epidemiological or socio-economic contexts. Annual cost per patient is separately gathered for an LPC and a HPC. The costs are adjusted to reflect full opportunity costs and the government and societal perspectives as in the case of data for the Markov models.

The annual number of patients using VCT and STD in an LPC and a HPC over the period 2007-2020 is obtained on the basis of estimates of the proportion of

patients benefiting from an intervention in the country. This proportion is then applied to the population of a given context. The annual number of patients for PMTCT and HAART over the period 2007-2020 is obtained directly from ASSA2008 AIDS model projections.

In socio-economic contexts, the annual cost per patient is collected in the literature in relevant contexts. The annual cost per patient is separately gathered for a rural context and an urban context. The annual number of patients using PMTCT, HAART FOR ADULTS and HAART FOR CHILDREN in a rural context and an urban context over the period is obtained directly from model projections. As in epidemiological contexts, the annual cost per patient is applied to estimate the cost over the period.

6.5 Data analysis, uncertainty and limitations of the methodology

This section deals with the analysis of the data. It explains how Markov and epidemiological projection models were used in the analysis and how uncertainty was handled and finally, it presents the limitations of the methodology.

6.5.1 Data analysis with Markov model

In the Markov model, data are analysed using TreeAge Pro software. Cohort simulation is conducted. A hypothetical cohort of 100,000 patients is applied to different transition probability matrices corresponding to the time horizon of the analysis. The outcomes of the simulation are the number of patients surviving in different HIV/AIDS states over the lifetime of the cohort. The cost and the effectiveness collected from the literature are applied to patients in HIV/AIDS states and the results are summed up. The cost and effectiveness of a given HIV/AIDS intervention in two contexts are compared.

The comparison of HIV/AIDS interventions is done using the ACER and the ICER. The ACER is used for comparison of HIV/AIDS interventions across contexts which do not take USUAL CARE into account, while ICER is used for comparisons of HIV/AIDS interventions involving USUAL CARE. In the latter comparison, the

ICER of an HIV/AIDS intervention compared to USUAL CARE is calculated in each context and the ICERs of that intervention across contexts are compared.

The extent to which the CE of an HIV/AIDS intervention in one context compares with the CE in another context is measured by comparing the ACER or ICER of that intervention in two contexts. When an ACER or ICER of an HIV/AIDS intervention in context one expressed as percentage of the ACER or ICER of that intervention in context two is less (more) than 100%, that HIV/AIDS intervention is more (less) cost-effective in the former context. The farther the percentage is below (above) 100%, the greater (lesser) is the CE of that HIV/AIDS intervention in context one.

6.5.2 Data analysis with epidemiological model

The number of patients in the Markov model in different HIV/AIDS states is one of the most important determinants of the cost and effectiveness of interventions. According to the Markov model, a change in these numbers over time is only due to death rather than migration and new births. Since one cannot ignore migration and new births when modelling population over a long period, this study compared cost-effectiveness from a different perspective by using epidemiological models which take deaths, migrations, and new births into account in modelling.

In this respect, epidemiological models are used to compare HIV/AIDS interventions which involve USUAL CARE. Projections of the annual health outcomes of HIV/AIDS interventions in terms of infections, deaths and life-years are recorded for the period 2007-2020 for USUAL CARE and a specific HIV/AIDS intervention. The effectiveness of an HIV/AIDS intervention is measured as infections averted, death averted and life years gained relative to USUAL CARE. The annual number of patients in an LPC and a HPC from 2007 to 2020 are projected using the ASSA2008 AIDS model for each of the modelled HIV/AIDS interventions. The projected number of patients for each HIV/AIDS intervention is also used for the intervention's USUAL CARE. In a rural and an urban context, the annual numbers of patients over the period 2007-2020 are projected by the SPMS for each of the modelled HIV/AIDS interventions. SPMS also projects the

annual number of patients in a rural context and an urban context in the case of USUAL CARE (absence of intervention).

The cost of HIV/AIDS interventions are estimated based on the annual number of patients using such interventions for the period of interest, namely 2007-2020. For an HIV/AIDS intervention, these numbers are estimated based on the guidelines of HIV/AIDS interventions and the usage rate (in epidemiological contexts) or directly obtained from the projection models (in socio-economic contexts). The costs of USUAL CARE for patients who use a specific HIV/AIDS intervention are estimated under the assumption that these patients would use USUAL CARE had there not been such an HIV/AIDS intervention.

The ICER is used to compare the CE of an HIV/AIDS intervention in one context with the ICER of the same intervention in another context. As in the case of Markov modelling explained above, the ICER of an HIV/AIDS intervention compared with USUAL CARE is calculated in each context and the ICERs of that intervention across contexts are compared.

6.5.3 Uncertainty and limitations of the methodology

Uncertainty is usually present in these types of analysis. Two types of analysis of uncertainty are conducted, probabilistic sensitivity analysis in the Markov model and scenario analysis in the projection models. Probabilistic sensitivity analysis considers all parameters in a model to be random variables, with specific probability distributions. One thousand random samples were drawn from the distribution of these parameters, average cost and effectiveness were calculated from these samples and the ICER or ACER was used to compare interventions.

Scenario analysis is conducted to assess the comparability of the CE of HIV/AIDS interventions across contexts in case of changes in some parameters. Specifically, scenario analysis is conducted to assess changes in the conclusion of the base-case analysis in case of a drop in adherence, in case of different discount rates and in case of the use of lower and upper bound cost-estimates.

Turning to the limitations of the methodology, it is acknowledged that modelling can only depict part of reality. AIDS models in particular, no matter how well they are modelled, may not capture the full reality and dynamics of HIV/AIDS. Other CE methodological limitations such as possible inaccuracy in assumptions, data and other issues have been surveyed by Raftery (1999) and referred to in the review of CE evidence in Africa (Creese *et al.*, 2002; Walker, 2003). Despite the shortcomings of modelling, it has become an important tool in advising policy makers in situations of uncertainty.

Chapter summary

In conclusion, this chapter presented the methodology used in this study, consisting of Markov modelling and epidemiological projection models in each context. The latter projection models are used to make assumptions about future progression in HIV/AIDS states. Two types of uncertainty are conducted, one that considers uncertainty on all parameters and another which includes scenario analysis on the basis of potential trends in adherence to HIV/AIDS interventions. This chapter outlined the general methodology; specific details are presented in the analysis chapters. The analysis chapter comparing the CE of HIV/AIDS interventions in epidemiological contexts using Markov models follows.

Chapter 7 : Cost-effectiveness of HIV/AIDS interventions in low and high HIV prevalence contexts

This chapter compares the CE of HIV/AIDS interventions across an LPC and a HPC. In each context, a hypothetical cohort of 100,000 patients in an HIV/AIDS intervention is followed up over time by means of a Markov states transition model. The proportions of patients, the costs and the quality of life data in various HIV/AIDS states, are collected from the literature. The effect of the interaction between an HIV/AIDS intervention and the context on the CE of such an intervention is taken into account. This is done by collecting the evidence in that context and modelling transitions in HIV/AIDS states over time as per trends suggested by the ASSA2008 AIDS model projections in that context. The effectiveness is measured in terms of survival or survival adjusted for the quality of life (QALYs). The CE of an HIV/AIDS intervention is compared across an LPC and a HPC using the ACER of that intervention in each context. Section one elaborates on the methods used; section two presents the results; and section three discusses the results.

7.1 Methods

Markov states transition models are constructed for each of the modelled interventions. Transitions probabilities, costs and quality of life data are collected from the literature, after which a sensitivity analysis is conducted.

7.1.1 Markov models

A pair of Markov models is constructed for each of the four interventions: voluntary counselling and testing (VCT), sexually transmitted diseases (STD), Prevention of Mother- to-Child Transmission (PMTCT) and treatment with highly active antiretroviral drugs (HAART). One Markov model tracks a hypothetical cohort of 100,000 patients in various HIV/AIDS states over the lifetime of the cohort in an LPC. Another Markov model does the same in a HPC. The Markov states transition model was explained in Chapter 6.

Briefly, the model represents patients in HIV/AIDS states in short and successive periods of the interventions' time horizon. The model determines the costs/health outcomes of an HIV/AIDS state by applying the HIV/AIDS state's costs/health outcomes to the number of patients in that HIV/AIDS state. Patients in each HIV/AIDS state are obtained by means of the proportion of patients, called transition probabilities, that usually falls in that HIV/AIDS state from other states when a cohort of patients is followed up. The cost and health outcomes of any one period of the successive periods are obtained by summing over costs/health outcomes of HIV/AIDS states in that period. The cost/health outcomes of the model over the term of analysis are obtained by summing over cost/health outcomes of successive periods.

To track a cohort of patients over time in prevention interventions (VCT, STD, and PMTCT), four HIV states are used: "non-infected", "infected with no AIDS", "infected with AIDS" and "dead". The state "infected with no AIDS" refers to the state in which patients are infected but not yet in need of antiretroviral drugs as per 2007 guidelines (below CD4 counts 200)¹⁶. The state "infected with AIDS" refers to the state when infected patients are in need of treatment.

While the main purpose of prevention interventions is to avoid new infections, avoiding costly and worse health outcomes in subsequent use of treatment interventions have also been acknowledged as benefits of prevention. To show these benefits, treatment-relevant HIV/AIDS states are added to the Markov state transition structure of prevention interventions.

A hypothetical cohort of 100,000 patients is assumed to start in a "non-infected" HIV/AIDS state and is followed up (simulated) in each prevention intervention over the lifetime of the cohort, that is, when almost all patients are dead. At one time in the future (the lifetime of the cohort) all patients who transit to the state "dead" do not transit any more. Therefore, eventually, all patients will accumulate in the "dead" state. The lifetime in the model is assumed to be reached when at least 95% of the cohort is dead. In each of the 3-month

¹⁶ These guidelines have changed since 2011 but the analysis here considers 2007 guidelines because of the absence of systematic cost and effectiveness data for the 2011 guidelines. The effect of these guidelines is however, discussed outside of modeling.

successive periods, some patients remain in the “non-infected” state, others move to “infected” and still others to “AIDS”. A typical Markov cycle tree structure for prevention intervention is shown in Appendix 1 (p.245).

In HAART intervention, the Markov state transition model tracks a cohort of patients in three HIV/AIDS states, namely, “non-AIDS”, “AIDS” and “death”. “Non-AIDS” refers to the state when patients are infected but have improved their CD4 count above the treatment threshold (CD4 count >200). “AIDS” refers to the state when patients have reached a serious stage of the illness, with a lot of serious opportunistic infections (CD4 count below 200). A hypothetical cohort of 100,000 patients is assumed to start in the “AIDS” state, and, in a 3-month period, some members remain in the same health state, while others move to the “non-AIDS” state in response to treatment, and still others to the “dead” state. Strata of CD4 counts are used to depict important stages of HIV progression in line with evidence that CD4 count is a major predictor of HIV progression (Egger *et al.*, 2002; Hogg *et al.*, 2001), health outcomes and costs. A typical Markov cycle tree structure for treatment interventions is presented in Appendix 2 (p.246).

The structure of the Markov model for a given intervention is assumed to be the same regardless of whether the intervention is conducted in an LPC or in a HPC. For example, the four HIV/AIDS states defined for a typical prevention intervention in an LPC are the same for that intervention in a HPC. Similarly, the 3-month transition period considered for a given intervention in an LPC applies to the same intervention in a HPC.

The lifetime (until at least 95% of the cohort is dead) costs, health outcomes and CE of HIV/AIDS interventions are simulated. The model tracks or simulates these costs and health outcomes in successive 3-month periods for a cohort of 100,000 patients in each context since 2007. The starting time for the analysis is motivated by the fact that this is when HIV/AIDS started receiving proper attention from the South African Government. The simulation is expected to estimate the economic implications of such commitment. To take account of the interaction between an HIV/AIDS intervention and the context, the proportion of

patients in HIV/AIDS states in subsequent 3-month periods are pegged on the ASSA2008 AIDS model projections (see Appendix 15 for more on this, p. 259).

7.1.2 Data and analysis

The transition probabilities (proportions) of patients in HIV/AIDS states from other HIV/AIDS states are gathered from the literature, notably HIV/AIDS cohort studies. Transition rates reported for periods other than 3 months are adjusted to take account of the 3-month period used in the Markov model. The rates, that is, the number of patients who move to a given HIV/AIDS state in a period of time, are converted into a 3-month transition probability using the formula $p = 1 - e^{-rt}$ suggested in the literature (Sonnenberg and Beck, 1993:330) where p is the transition probability, r is the rate or the number of patients who transit in a period of time, t . The time is transformed in the number of 3-month periods either through multiplication or division depending on whether t is greater or less than a 3-month period. Table 7:1 provides a summary of transition probabilities used in the base-case analysis for VCT and treatment of STD.

Table 7:1 Transition probabilities data for the base-case comparison: VCT and STD

VCT	Low HIV prevalence context		High HIV prevalence context	
Transition probability	Base-case Value	Evidence sources	Value	Evidence sources
Non-infected to non-infected	0.98	Model derived	0.95	Model derived
Non-infected to infected with no AIDS	0.00639	ASSA (2011)	0.0041	Rehle <i>et al.</i> (2007)
Non-infected to infected with AIDS	0.0001	Rehle <i>et al.</i> (2007)	0.00006	ASSA (2011)
Non-infected to death	0.0001	Anderson <i>et al.</i> (2006)	0.00002	Anderson <i>et al.</i> (2006)
Infected with non-AIDS to infected with no AIDS	0.99	Model derived	0.98	Model derived
Infected with non-AIDS to infected with AIDS	0.0003	Stover (2009)	0.001	ASSA (2011)
Infected with non-AIDS to death	0.0005	Badri <i>et al.</i> (2006)	0.0009	Rehle <i>et al.</i> (2007)
Infected with AIDS to infected with non-AIDS	0.0001	Model derived	0.0001	Model derived
Infected with AIDS to infected with AIDS	0.92	Badri <i>et al.</i> (2006)	0.98	Cleary <i>et al.</i> (2006)
Infected with AIDS to death	0.05	Cleary <i>et al.</i> (2004)	0.09	Bachman (2006)
STD				
Non-infected to non-infected	0.992	Model derived	0.985	Model derived
Non-infected to infected with no AIDS	0.0077	Johnson (2008)	0.0145	Auvert (2001)
Non-infected to infected with AIDS	0.0001	ASSA (2011)	0.0001	Johnson & Budlender (2001)
Non-infected to death	0.00022	Anderson <i>et al.</i> (2006)	0.00042	Anderson <i>et al.</i> (2006)
Infected with non-AIDS to infected with non AIDS	0.95	Model derived	0.91	Model derived
Infected with non-AIDS to infected with AIDS	0.009	Johnson <i>et al.</i> (2005)	0.11	Gilson <i>et al.</i> (1996)
Infected with non-AIDS to death	0.003	Badri <i>et al.</i> (2006)	0.009	Model derived
Infected with AIDS to infected with non-AIDS	0.0001	Cleary <i>et al.</i> (2004)	0.00001	Badri <i>et al.</i> (2004)
Infected with AIDS to infected with AIDS	0.90	Model derived	0.92	Model derived
Infected with AIDS to death	0.028	Stover (2009)	0.09	Stover (2009)

The 3-month data adjustment reported for VCT and STD is also reported for PMTCT and HAART. Table 7:2 shows such data.

Table 7:2 Transition probabilities data for the base-case comparison: PMTCT and HAART

PMTCT	Low HIV prevalence context		High HIV prevalence context	
Transition probability	Base-case Value	Evidence sources	Value	Evidence sources
Non-infected to non-infected	0.92	Model derived	0.85	Model derived
Non-infected to infected with no AIDS	0.06	Skordis & Natrass(2002)	0.08	Wilkinson <i>et al.</i> (2000)
Non-infected to infected with AIDS	0.0001	Soorapath <i>et al.</i> (2006)	0.0001	Stover(2009)
Non-infected to death	0.001	Anderson <i>et al.</i> (2006)	0.0042	Anderson <i>et al.</i> (2006)
Infected with non-AIDS to infected with no AIDS	0.85	Model derived	0.79	Model derived
Infected with non-AIDS to infected with AIDS	0.006	Stover (2009)	0.009	Stover (2009)
Infected with non-AIDS to death	0.06	Cleary <i>et al.</i> (2004)	0.09	Boulle <i>et al.</i> (2002)
Infected with AIDS to infected with non-AIDS	0.0001	Badri <i>et al.</i> (2006)	0.00001	Boulle <i>et al.</i> (2002)
Infected with AIDS to infected with AIDS	0.091	Model derived	0.90	Model derived
Infected with AIDS to death	0.09	Badri <i>et al.</i> (2006)	0.11	Granich <i>et al.</i> (2012)
HAART				
Non-AIDS to non-AIDS	0.960	Model derived	0.985	Model derived
Non-AIDS to AIDS	0.0482	Badri <i>et al.</i> (2006)	0.0615	Boulle <i>et al.</i> (2002)
Non-AIDS to deaths	0.000612	Cleary <i>et al.</i> (2004)	0.019	Natrass & Geffen (2005)
AIDS to non-AIDS	0.0001	Ferrer <i>et al.</i> (2004:1727)	0.00001	Granich <i>et al.</i> (2012)
AIDS to AIDS	0.920	Model derived	0.960	Model derived
AIDS to death	0.039	Bachman <i>et al.</i> (2006)	0.055	Walensky <i>et al.</i> (2011)

The costs in HIV/AIDS states are also collected from the literature. This chapter only considers the costs that reflect the full opportunity costs of each intervention. Since the South Africa Government funds two-thirds of the HIV/AIDS response (Stewart, 2010), the base-case value analysis is considered from the government perspective. However, a societal perspective is also analysed to facilitate comparison of results with other studies as per CE expert recommendations (Gold *et al.*, 1996:166). A societal perspective takes account of full opportunity costs, that is, interventions' costs and patients' costs. A societal perspective includes estimates of transport, funeral and waiting time costs in addition to government perspective costs. Real costs are used in the analysis using 2007 prices and are discounted at 3% in line with the recommendation from CE analysis experts (Gold *et al.*, 1996). Undiscounted results are also reported for the sake of comparison with studies that have reported such results. All analyses are performed using TreeAgePro (DATA TM) software and data are transferred to excel for graphical and numerical analyses (see Appendix 16 for an example on p.261). The baseline cost data are presented in Table 7:3.

Table 7:3 Three-month cost data for the base-case comparison (in US\$)

HIV state	Low HIV prevalence context			High HIV prevalence context		
VCT	GP	SP	Evidence sources	Value GP	SP	Evidence sources
Non-infected	30	40	McConnell <i>et al.</i> (2005), Geffen <i>et al.</i> (2003)	30	40	McConnell <i>et al.</i> (2005), Geffen <i>et al.</i> (2003)
Infected with no AIDS	30	40	Walensky <i>et al.</i> (2011)	30	40	Walensky <i>et al.</i> (2011)
AIDS	365	465	Bachmann (2006)	365	465	Bachmann (2006)
Deaths	0	704	Case <i>et al.</i> (2006)	0	704	Case <i>et al.</i> (2006)
STD	GP	SP	Evidence sources	GP	SP	Evidence sources
Non-infected	17.5	28.5	Vickerman <i>et al.</i> (2006)	17.5	28.5	Vickerman <i>et al.</i> (2006)
Infected with no AIDS	17.5	28.5	Vickerman <i>et al.</i> (2006)	17.5	28.5	Vickerman <i>et al.</i> (2006)
AIDS	365	465	Badri <i>et al.</i> (2004)	365	465	Badri <i>et al.</i> (2004)
Deaths	0	704	Case <i>et al.</i> (2008)	100	704	Case <i>et al.</i> (2008)
PMTCT	GP	SP	Evidence sources	GP	SP	Evidence sources
Non-infected	100	120	Soorapath <i>et al.</i> (2006)	100	120	Soorapath <i>et al.</i> (2006)
Infected with no AIDS	100	120	Soorapath <i>et al.</i> (2006)	100	120	Soorapath <i>et al.</i> (2006)
AIDS	365	465	Cleary <i>et al.</i> (2004)	365	465	Cleary <i>et al.</i> (2004)
Deaths	0	704	Case <i>et al.</i> (2008)	100	704	Case <i>et al.</i> (2008)
HAART	GP	SP	Evidence sources	GP	SP	Evidence sources
Non-AIDS	100	150	Badri <i>et al.</i> (2006)	100	150	Badri <i>et al.</i> (2006)
AIDS	365	465	Cleary <i>et al.</i> (2004)	365	465	Cleary <i>et al.</i> (2004)
Deaths	0	704	Case <i>et al.</i> (2008)	100	704	Case <i>et al.</i> (2008)

NB: Societal perspective (SP) costs are estimated based on the available evidence on the average cost of transport, waiting time and funeral costs in South Africa.

The health outcome in an HIV/AIDS state is calculated based on the duration and quality of life of that state. To this end the chapter collects the quality of life data from the South African literature (O’Keefe & Wood 1996; Jelsma *et al.*, 2005; Louwagie *et al.*, 2007). Quality of life data in South Africa has been collected using instruments that contain descriptive questions whose answers provide the measure of overall health. The community average health related quality of life (HRQoL) has been taken as the average HRQoL from the representative sample.

In CE analysis, however, individual responses need to reflect preferences. Individual responses can be transformed into preference measures or utility indices using an algorithm that predicts a utility score for a set of responses from an individual. The prediction model was developed based on the responses in a sample of the UK population (Dolan, 1997; Dolan *et al.*, 1995). The same algorithm has been used to produce the value of the responses from the instrument used in South Africa. Using a Euroqol, an instrument that asks questions about mobility and pain/discomfort in a health state, Jelsma *et al.* (2005) produced values of quality of life for patients receiving HAART over a one-year period in Cape Town. Using the same instrument in the Free State, Louwagie *et al.* (2007) analysed the value of quality of life for HIV/AIDS patients receiving and not receiving treatment. This chapter uses these values in different health states of the model. The base-case values used in the analysis are illustrated in Table 7:4.

Table 7:4 Quality of life data

HIV state	Low HIV prevalence context		High HIV prevalence context	
VCT	Base case value (BCV)	Evidence base	Base case Value (BCV)	Evidence base
Non-infected Infected with no AIDS AIDS Deaths	1 0.90 0.60 0	Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007)	1 0.90 0.60 0	Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996)
STD	BCV	Evidence base	BCV	Evidence base
Non-infected Infected with no AIDS AIDS Deaths	0.90 0.90 0.60 0	Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007)	0.90 0.90 0.60 0.00	Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996)
PMTCT	BCV	Evidence base	BCV	Evidence base
Non-infected Infected with no AIDS AIDS Deaths	0.90 0.80 0.60 0	Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007)	0.90 0.80 0.60 0	Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996)
HAART	BCV	Evidence base	BCV	Evidence base
Non-AIDS AIDS Death	0.90 0.60 0	Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O'Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007)	0.90 0.60 0	Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O'Keeffe & Wood (1996)

N.B: Utility weights are assumed to be the same across an LPC and a HPC. BCV means base-case values.

7.1.3 Assumptions

Since the activities of interventions are the same, the costs in the same HIV/AIDS state are assumed to be the same across an LPC and a HPC, as is the quality of life. However, the simulation includes an assumption of economies of scales in HIV/AIDS states, with unit costs moving in an inverse relationship with the number of patients in HIV/AIDS states. Due to the unavailability of evidence regarding the effects of the changes in the PMTCT and HAART guidelines in 2010 and 2011, the analysis is conducted under the assumption of the 2007 guidelines. The possible effects of these changes are discussed outside of the modelling. Uncertainty, expected to arise from any parameter, is handled by probabilistic sensitivity analysis in which lognormal distributions and triangular distributions were used for cost and effectiveness values, respectively.

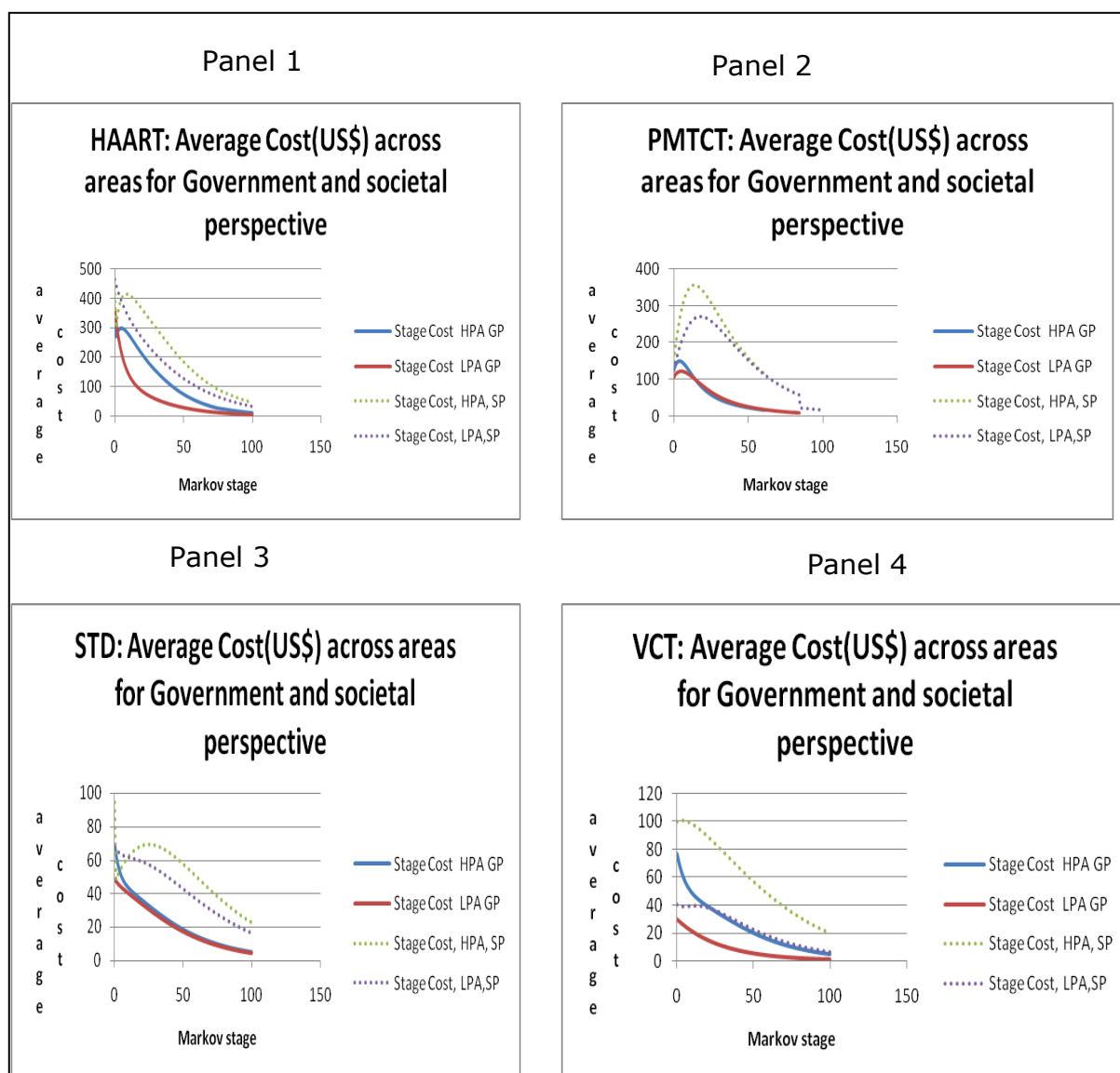
7.2 Results

This section presents the results. It distinguishes the costs, effectiveness, and CE results, in this presentation.

7.2.1 Costs

In order to understand the CE of intervening in a HPC and an LPC, it is useful to analyse the data relating to the cost and the effectiveness of intervening in these contexts separately. This analysis starts with the costs.

The costs of intervening in an LPC and a HPC depend on the distribution of patients and the unit cost in HIV/AIDS states in these contexts. Assuming an equal unit cost in the same HIV/AIDS state across an LPC and a HPC implies that the pattern of costs depends on the distribution of patients in HIV/AIDS states across contexts. The average cost results of this analysis are summarised in Figure 7:1.

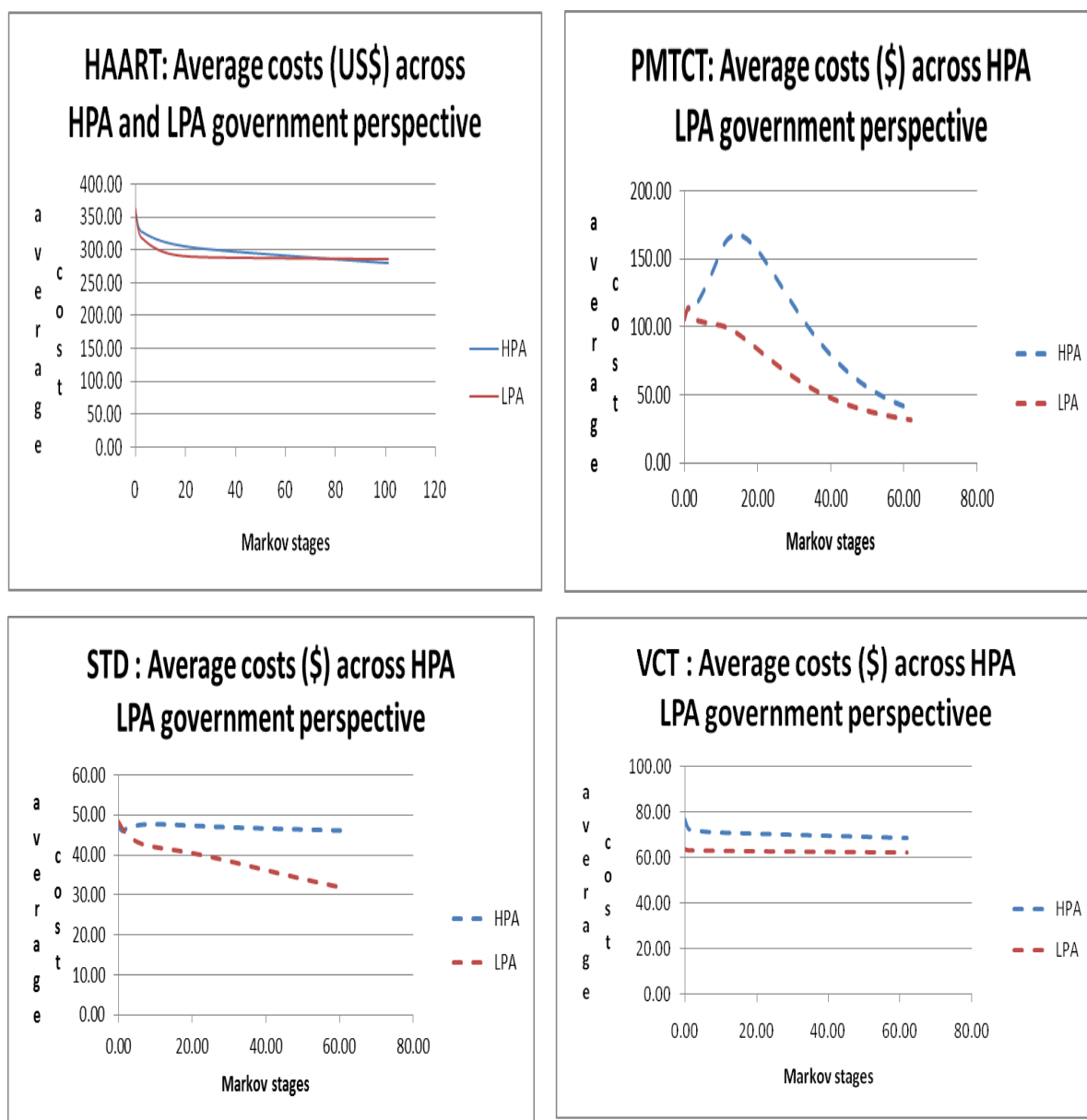


LPA (low prevalence area or context), HPA (high prevalence area or context). Source: based on the results of Markov models' simulations.

Figure 7:1 Stage costs in an LPC *versus* a HPC

As expected, the average cost is greater in a HPC than in an LPC. The difference in cost arises because over time, relatively more patients are in costly HIV/AIDS states in a HPC than they are in an LPC. However, the assumption of the same set up of interventions across the contexts implies similar fixed and variable resources in HIV/AIDS states. An implication of this assumption is that different distributions of patients in these HIV/AIDS states might result in different unit costs because of economies of scale. The chapter investigated this question by assuming an inverse relationship between the growth of the number of patients in HIV/AIDS states and the unit costs in the HIV/AIDS states. Figure 7:2

presents the patterns of average costs for the government perspective which would be similar to the pattern for the societal perspective.



LPA (low prevalence area or context), HPA (high prevalence area or context). Source: Based on the results of Markov models' simulations.

Figure 7:2 Costs of intervening in an LPC and a HPC

The results suggest different patterns in average costs across an LPC and a HPC with PMTCT and STD exhibiting the greatest differences. In comparison with the previous discussions in this chapter, an assumption of economies of scale changes the cost levels, but not the pattern across an LPC and a HPC except for VCT. It is worth noting the greater average costs for prevention intervention

than would be expected. This result is due to the fact that, the chapter included subsequent benefits in treatment of HIV/AIDS states for prevention interventions assuming linkages of prevention to treatment. Table 7:5 presents the results of a comparison of the costs of HIV/AIDS interventions using numbers rather than graphs.

Table 7:5 Comparison of average lifetime costs across an LPC and a HPC (costs discounted at 3%, government perspective)

HIV/AIDS Intervention	LPCC	HPCC	Costs in an LPC as % of the costs in a HPC
VCT 95% confidence interval	400 (62-1898)	522 (98.77-2095)	76%
STD 95% confidence interval	525 (483-4490)	430 (90-1836)	122%
PMTCT 95% confidence interval	489 (67-2533)	263 (432-1379)	185%
HAART 95% confidence interval	1257 (146-6879)	9092 (8924-9647)	14%

Source: Author, based on the results of Markov models' simulations. LPCC: Low prevalence context's costs, HPCC: High prevalence context's costs.

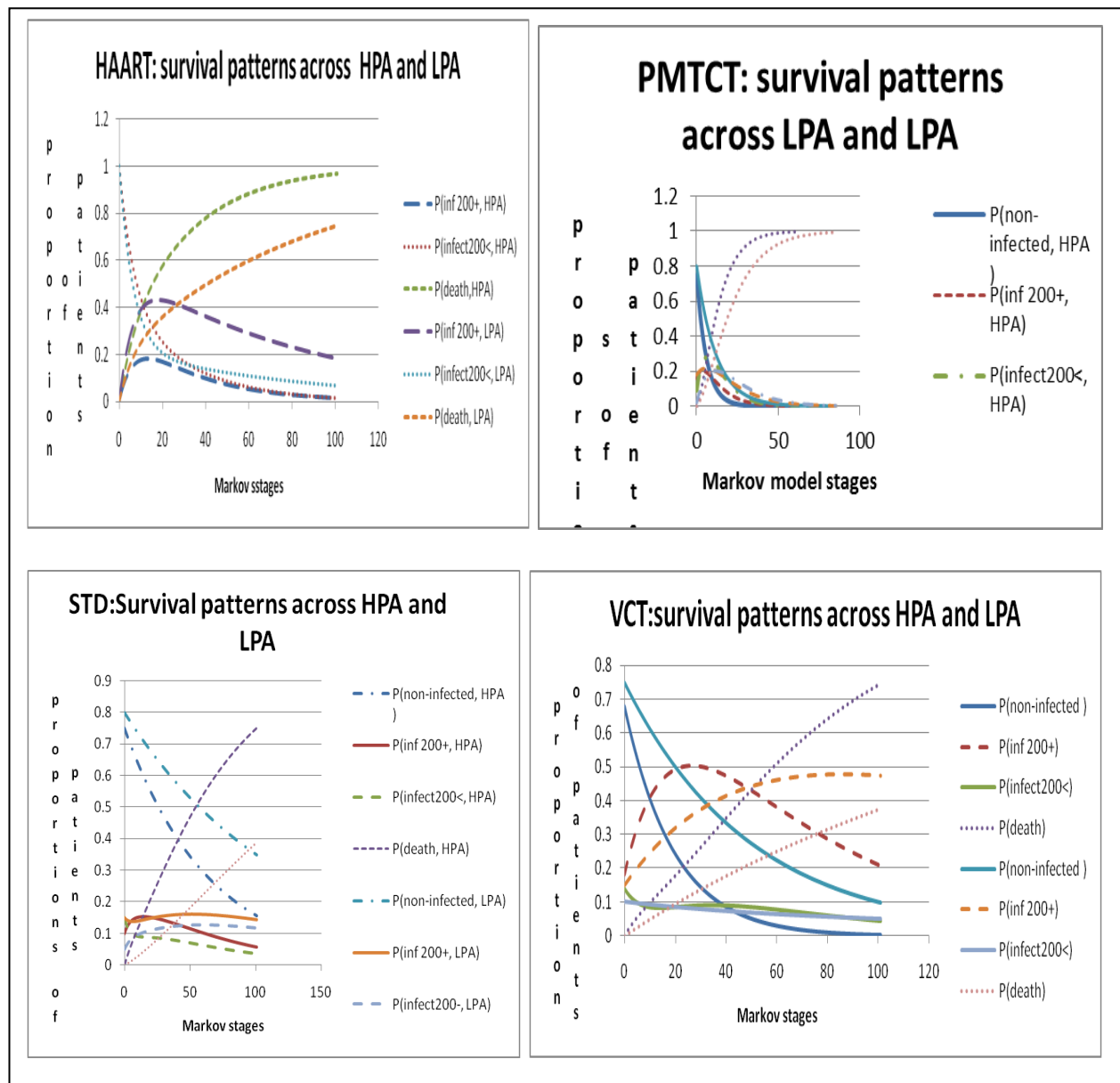
The Table shows that the average cost of STD and PMTCT are greater in an LPC than they are in a HPC, while the average cost of VCT and HAART are less in an LPC than they are in a HPC. Table 7:5 also shows that the costs of an HIV/AIDS intervention in an LPC as a percentage of its costs in a HPC are different across interventions, ranging from 14% to 122%. This result indicates that the extent of costs (how close the cost of an HIV/AIDS intervention in one context as a percentage of its own cost in another context is to 100%) is also different across HIV/AIDS interventions. It is worth noting, however that these estimates have very wide confidence intervals. For instance, the lower bound of the VCT costs is US\$62 with an upper bound of US\$1898 while the average is US\$400. The variation of the average value farther away from the upper and lower bound estimates indicates limited accuracy of the estimates.

7.2.2 Effectiveness

This section presents the effectiveness of HIV/AIDS interventions across an LPC and a HPC. It discusses effectiveness in terms of survival, and survival adjusted with quality of life.

7.2.2.1 Survival

This section analyses effectiveness by comparing survival differences across the contexts. The results of these comparisons are presented in Figure 7:3.



Source: Author, based on the results of Markov models' simulations. Key: LPA (low prevalence area or context), HPA (high prevalence area or context), infect200+ (infected with CD4 count above 200), infect200< (infected with CD4 count below 200).

Figure 7:3 Survival patterns across an LPC and a HPC in South Africa

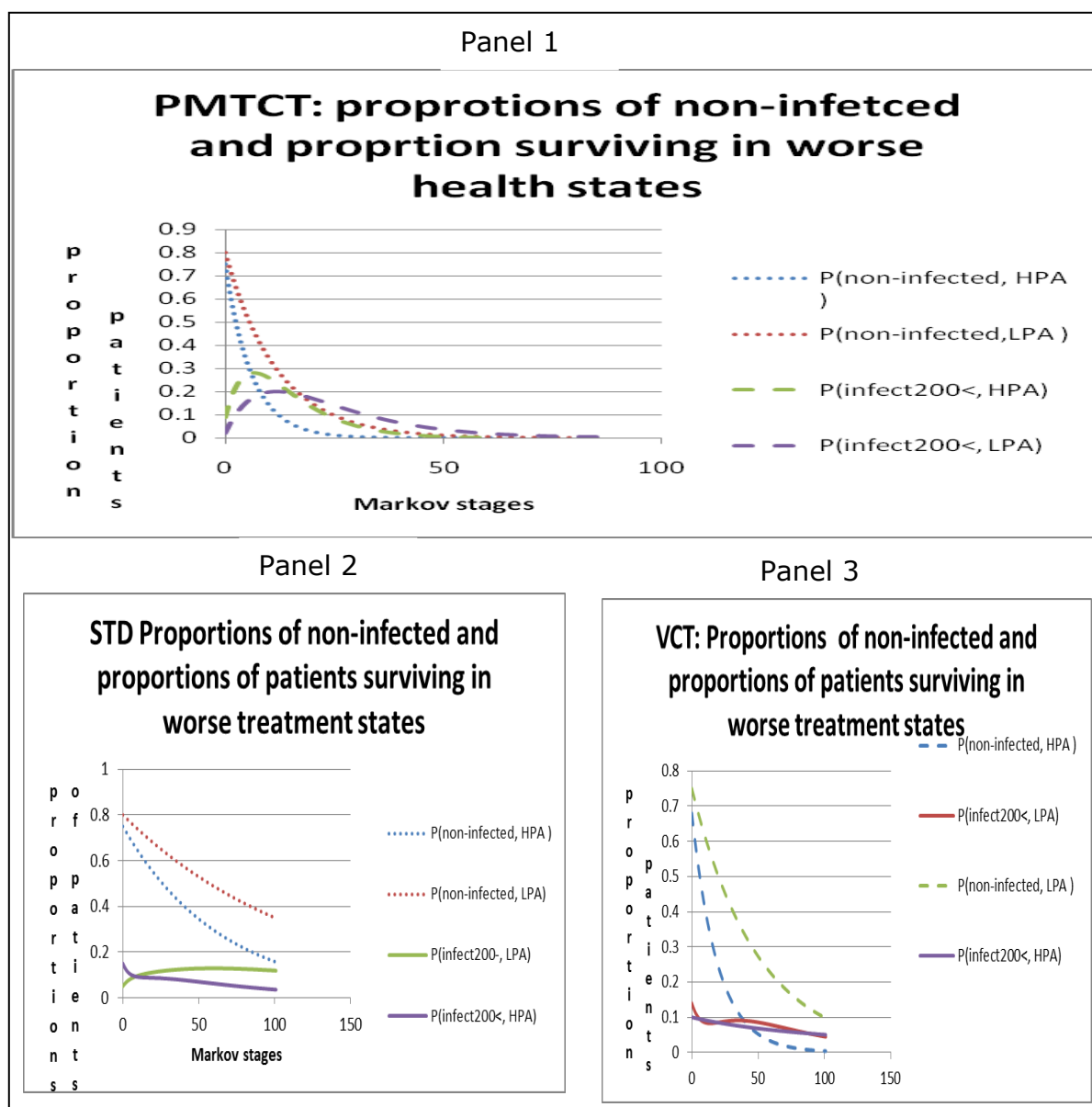
As shown in Figure 7:3, the patterns of survival across an LPC and a HPC are quite different, with the greatest differences apparent in HIV/AIDS states "non-infected" and "dead". The smallest differences are observed in the HIV/AIDS state "infected" (CD4 200-). Moreover, the pattern of survival appears to be

different across HIV/AIDS interventions. The results show that in general, survival is greater in an LPC than in a HPC.

While it might be speculative to point to the exact reasons for the differences, the results reflect that the same intervention results in different survival outcomes across an LPC and a HPC. These results partially answer the study's initial question of whether or not the interaction of the intervention and the context has an effect on cost-effectiveness. These results show that this might be the case and hence suggest that policy makers in South Africa should take account of the prevalence level in contexts when implementing HIV/AIDS interventions.

Differences in intervention outcomes can be explained by a number of social theories of health behaviour according to which differences in health status depend on people's perception of risk which in turn depends on personal characteristics (Becker, 1974) or the characteristics of the society in which they live (Bandura, 1986). On the other hand, empirical research has reached different conclusions about how interventions interact with cultural norms (Airhihenbuwa, 2004). Some studies have concluded that risk behaviour reduction would be greater for people witnessing a real threat from an epidemic, in this case a HPC (Geoffard & Phillips, 1996; Sweat *et al.*, 2000:113). While some of these conclusions may be relevant to South Africa, it seems that the effectiveness of an HIV/AIDS intervention depends on the area of such intervention.

In comparing the effectiveness of intervening in an LPC and a HPC using survival for prevention interventions, we cannot ignore the fact that the latter's main purpose is to prevent new infections. However, nor can we ignore the evidence that beneficiaries of different prevention interventions fare differently in treatment interventions (Sweat *et al.*, 2000). To reflect these two facts, the chapter compared the proportion of "non-infected" patients over time with the proportion of patients in treatment-relevant HIV/AIDS states across an LPC and a HPC. Figure 7:4 shows these results.



Source: Author, based on the results of Markov models' simulations. Key: LPA (low prevalence area or context), HPA (high prevalence area or context), infect200+ (infected with CD4 count above 200), infect200< (infected with CD4 count below 200).

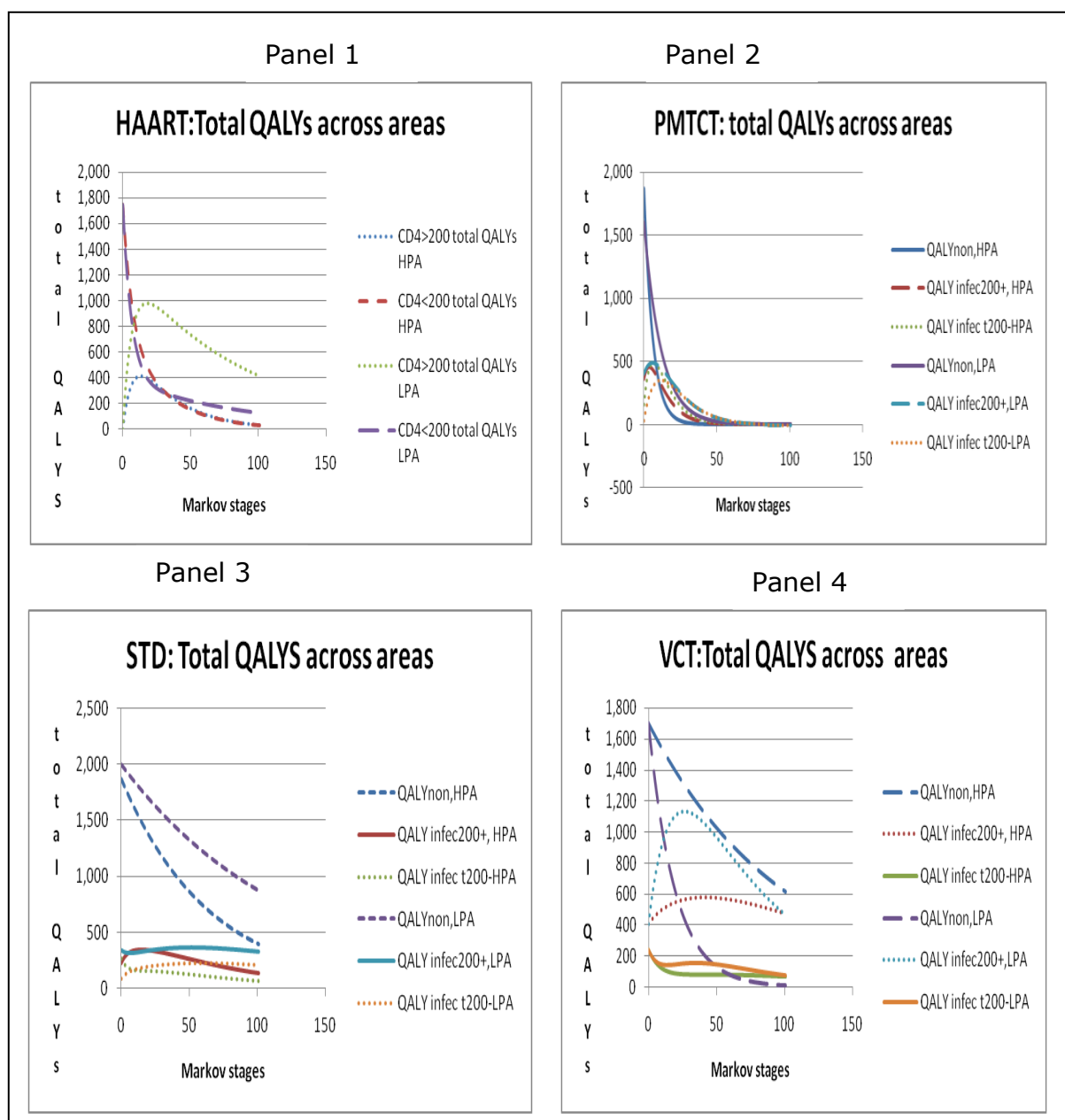
Figure 7:4 Proportions of non-infected, infected and proportions of patients surviving in treatment states

Figure 7:4 shows that over time an LPC produces a greater proportion of patients in "non-infected" and "infected CD4 200-" states than a HPC. Moreover, the figure depicts a more rapidly decreasing proportion of patients in "infected CD4 200-" in a HPC than it does for an LPC. In summary, this result suggests that intervening in an LPC with prevention interventions not only results in more infections averted but also in more future treatment benefits than in a HPC. Again, with interventions' activities being the same, this difference in results can

be attributed to differences in the interaction between the context type and the intervention.

7.2.2.2 Survival adjusted with quality of life

This section compared effectiveness using survival years adjusted with quality of life. Comparisons using this measure were motivated by the fact that two interventions might achieve same survival rates, but different quality of life. Multiplying survival years in a HIV/AIDS state with percent of perfect health in that HIV/AIDS state (considered as quality of life) yielded the number of perfect years of life across contexts, called quality adjusted life years (QALYs). Using QALYs as a measure of effectiveness of intervening in an LPC and a HPC, produced the results depicted in Figure 7:5.



Source: Author, based on the results of Markov models' simulations. Key: LPA (low prevalence area or context), HPA (high prevalence area or context), infect200+ (infected with CD4 count above 200), infect200< (infected with CD4 count below 200).

Figure 7:5 Comparison of QALYs across an LPC and a HPC

This Figure shows that QALY outputs are greater in an LPC than in a HPC. The greatest differences across contexts in total QALYs is observed for non-ARV interventions (STD and VCT) particularly in the HIV/AIDS state "non-infected". Once again, the fact that QALYs from the same intervention and on the same kinds of patients are different across contexts is indicative of the different effect on QALYs of the interaction between an intervention and the context of intervention.

While graphical analysis provides a picture of how the effectiveness of HIV/AIDS interventions compares across an LPC and a HPC, a comparison of differences in the extent of effectiveness requires a presentation of effectiveness in terms of numbers of QALYs. Table 7:6 shows and compares the effectiveness of HIV/AIDS interventions, expressing effectiveness in an LPC as a percentage of the effectiveness in a HPC.

Table 7:6 Comparison of average lifetime effectiveness of HIV/AIDS interventions across an LPC and a HPC (QALYs discounted at 3%)

HIV/AIDS Intervention	LPC E	HPC	QALYs in an LPC as % of QALYs in a HPC
VCT 95% confidence interval	5 (2-7)	4 (2-5)	125%
STD 95% confidence interval	5 (2-7)	4 (2-6)	125%
PMTCT 95% confidence interval	3 (2-3)	1 (0-1)	300%
HAART 95% confidence interval	3 (2-4)	2 (1-3)	150%

Source: Author, based on the results of Markov models' simulations. Keys: LPCE: low prevalence context's effectiveness, HPCE: high prevalence context's effectiveness.

The effectiveness results in epidemiological contexts show that the effectiveness of each HIV/AIDS intervention in an LPC, as a percentage of its effectiveness in a HPC, is greater than 100%. This result suggests that each of the modelled HIV/AIDS interventions is more effective in an LPC than it is in a HPC.

7.2.3 Cost-effectiveness

Having gained some understanding of the pattern of costs and effectiveness, it is now time to discuss the relative CE of intervening in an LPC and a HPC. This is analysed using, as per the literature, the ratio of cost to effectiveness, known as the CE ratio (CER). The results of Monte Carlo simulation for the government perspective are summarised in Table 7:7.

Table 7:7 Lifetime costs and effectiveness

Intervention	HPC C (\$)	HPCE (QALYs)	HPC ACER (\$/QALY)	LPC C (\$)	LPCE (QALYs)	LPC ACER (\$/QALY)	ACER in an LPC as % of ACER in a HPC
VCT Discounted 95% CI	522 (98.72-2095)	4 (2-5)	130.50	400 (62-1898)	5 (2-7)	80	61
Undiscounted 95% CI	1525 (375-5763)	10 (5-13)	152.3	1211.16 (483-4490)	5 (3-6)	242	
STD Discounted 95% CI	430 (90-1836)	4 (2-6)	107.50	525 (67-2533)	5 (2-7)	105.00	98
Undiscounted 95% CI	1291 (356-5084)	10 (5-14)	129.1	1743 (256-8445)	13 (6-18)	134.07	
PMTCT Discounted 95% CI	263 (144-460)	1 (0-1)	263	489 (170-2250)	3 (2-3)	163	61
Undiscounted 95% CI	789.44 (432-1379)	2 (1-3)	394.72	1211.16 (483-4490)	5 (3-6)	242.23	
HAART Discounted 95% CI	9092.72 (8924-9647)	2 (1-3)	846.36	1257 (146-6879)	3 (2-4)	635	75
Undiscounted 95% CI	24410 (24049-25030)	5 (3-7)	5424.60	2657 (493-13125)	2 (4-11)	1328.50	

Source: Author, based on the results of Markov models' simulations. LPCC: low prevalence context's cost, LPCE: low prevalence context's effectiveness, LPCACER: low prevalence context's average cost-effectiveness ratio, HPCACER: high prevalence context's average cost-effectiveness ratio.

The results in the Table show that prevention interventions result in greater QALYs and smaller costs than treatment interventions, regardless of the context in which they are conducted. For example, in a HPC, VCT has smaller costs of US\$130.50 per QALY (see column 4, row 2 in Table 7:7) while the corresponding value for HAART is US\$ 846.36 per QALY (see column 4, row 5 of Table 7:7. This result is in line with the literature (Canning, 2006). The results also indicate that intervening in a HPC with ARV-based interventions, namely, PMTCT and HAART, is less cost-effective.

Notable in the results is the different extent of the relative CE ratio across contexts and interventions. For example, across contexts, one notes that the average CE ratio for VCT in an LPC is 61% of the average CE ratio of the same intervention in a HPC. In fact, the average cost effectiveness ratio (ACER) in an LPC as a percentage of the ACER in a HPC is generally lower than 100%, as

shown in Table 7:8, which means that HIV/AIDS interventions are more cost-effective in an LPC than they are in a HPC. Furthermore, the average The CE ratio of VCT in a HPC is US\$130.50 per QALY, while it is about sevenfold, US\$ 846.36 per QALY, for HAART in the same context.

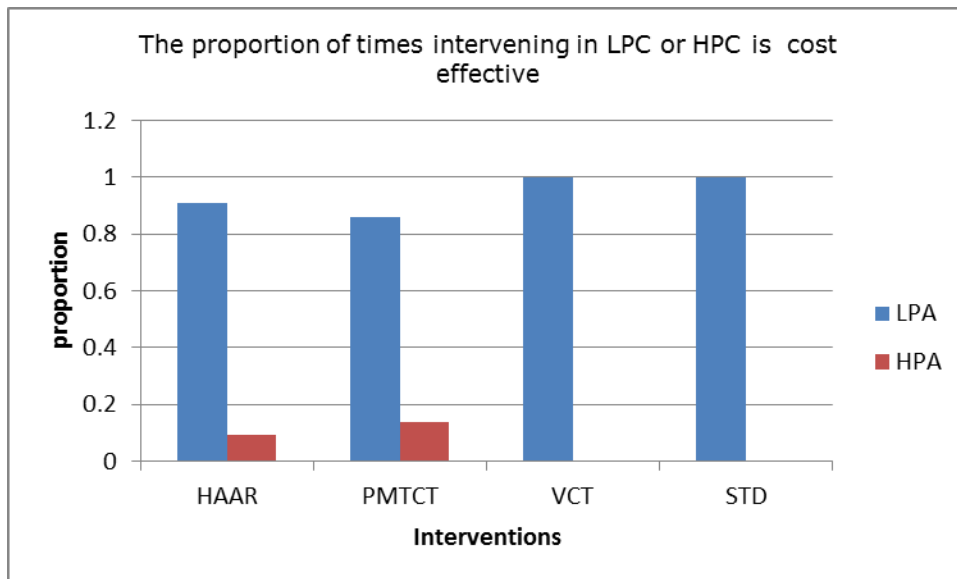
Table 7:8 Comparison of the extent of cost-effectiveness across contexts and across interventions in an LPC and a HPC (in US\$/outcome)

ACER in LPC per QALY	ACER in HPC per QALY	ACER in an LPC as % of ACER in a HPC
VCT		
80	130	61
STD		
105	107	98
PMTCT		
163	263	61
HAART		
635	846	75

Source: Author, based on the results of Markov models' simulations.

This result means that HIV/AIDS interventions are more cost-effective in an LPC than they are in a HPC since the ACERs in an LPC are lower than those in a HPC. It is interesting to note that despite these trends, the extent of CE is different across interventions. Specifically, VCT and PMTCT are more cost-effective in an LPC than any other intervention. The ACER of VCT and of PMTCT in an LPC is 61% of their respective ACERs in a HPC. While VCT and PMTCT are the most cost-effective in an LPC, STD is the least cost-effective in that context. The ACER of STD in an LPC is 98% of its ACER in a HPC.

The uncertainty surrounding these results is however, immense. The chapter sought to ascertain the robustness of the conclusion that intervening in an LPC is more cost-effective. Using 1,000 samples drawn from values of parameters distributions, the proportion of time that intervening in an area is cost-effective was obtained (see appendix 17 for more on p. 264). Figure 7:6 shows the results.



Source: Author, based on the results of Markov models' simulations.

Figure 7:6 Results of probabilistic sensitivity analysis

The results suggest that intervening in an LPC is more cost-effective than intervening in a HPC. As shown in Figure 7:6, the probability of achieving this outcome, arrived at through Monte Carlo simulation, results in expected values of costs and effectiveness which range between 90% and 100%.

For PMTCT, the above analysis was conducted utilising the guidelines used until 2010. These guidelines consisted of a single dose of Nevirapine around the time of birth combined with options to breastfeed or not breastfeed. A more expensive but more effective guideline was adopted in 2010 consisting of compound Zidovudine (AZT) from week 14 for infected mothers. Some evidence indicates that the new guidelines are effective but the way in which they affect CE depends on the relative increase in cost and effectiveness. While their effect on the CE ratio in an LPC and a HPC is incontestable, the pattern of CE across an LPC and a HPC does not change, given the unchanged dynamics of the interaction between intervention and contexts. The same argument applies to the more expensive but more effective new guidelines adopted in 2011 to provide antiretroviral drugs to patients whose CD4 counts falls below 350.

7.3 Discussion of the results

The evidence presented so far in this chapter has shown that modelled HIV/AIDS interventions are more cost-effective in an LPC than they are in a HPC. If HIV/AIDS interventions were equally cost-effective in an LPC and a HPC, the average CE ratio (ACER) of each intervention in an LPC as a percentage of its average CE ratio in a HPC would be 100%. The farther this percentage is below 100%, the more the intervention is cost-effective in an LPC and, the farther it is above 100%, the less the intervention is cost-effective in an LPC. The results have shown that the ACER in an LPC as a percentage of an ACER in a HPC is less than 100%, meaning that modelled HIV/AIDS interventions are generally more cost-effective in an LPC.

Another feature in the evidence is that the extent of CE is different across HIV/AIDS interventions. It is noted that, although all interventions are more cost-effective in an LPC, some are more cost-effective than others. For instance the results illustrate that HAART and STD are least cost-effective in an LPC, with its ACER in an LPC representing 75% and 98%, respectively of its ACER in a HPC.

These results mean that the CE of HIV/AIDS interventions not only depends on the context but also on the type of intervention. Reverting back to how the modelling of these results was conducted - with the same size cohort, same HIV/AIDS states and similar design of interventions - the results are expected to be the same. However, the opposite is observed. This observation answers the research question on whether or not the CE of HIV/AIDS interventions is influenced by the context in which they are implemented. The claim that the performance of HIV/AIDS interventions depends on contexts has featured in the literature for some time. However, thus far it has not been supported by sufficient, formal CE evidence; the evidence presented in this chapter therefore contributes to this body of knowledge.

Many factors explain why the CE of HIV/AIDS intervention might be different in different contexts. These factors influence the costs and effectiveness. Contextual and individual factors interact in a complex manner with HIV/AIDS

interventions to influence not only health outcomes but also costs. This interaction explains why these costs and health outcomes are different across contexts. Since an intervention is standard across the contexts, the prevalence of contextual and individual factors to a different degree in these contexts influences the health outcomes and the cost of intervention.

Furthermore, these factors explain why the extent of CE across HIV/AIDS interventions is also different. Since each HIV/AIDS intervention interacts in a unique way with these factors, the outcomes across interventions cannot be expected to be the same. The outcomes of such interactions are expected to depend on the intervention and explain why interventions achieve different levels of CE from one context to another.

Due to the fact that many factors are likely to influence the outcomes of interventions in different contexts, the empirical outcomes of such interaction can guide policy makers. The CE difference observed across contexts can possibly be understood from the patterns of its components, notably costs and effectiveness.

This analysis found that the effectiveness of HIV/AIDS interventions was greater in an LPC than a HPC. This could be explained by relatively smaller rates of infection in a cohort and therefore little progression to worse HIV/AIDS state in an LPC. However, Philipson & Posner (1993) predict more infections in an LPC due to limited information on the cost of infections.

The behaviour of the costs of HIV/AIDS interventions in an LPC relative to a HPC is even more complex. The costs of STD and PMTCT were found to be greater in an LPC than in a HPC while the opposite was found for VCT and HAART. The costs are expected to depend on the impact, since the activity of the intervention depends on the HIV/AIDS state. If more patients are found in worse HIV/AIDS states in one context than another, the costs are expected to be lower in an LPC. The costs could also increase as a result of usage. As the usage increases with greater knowledge of the dangers of the disease and the benefits of HIV/AIDS interventions, greater costs are expected in a HPC. However this is mere speculation in order to try and understand what could explain the

differences in costs across an LPC and a HPC. While there are specific trends in the costs of the modelled HIV/AIDS intervention across an LPC and a HPC, it is difficult to ascertain the reasons for the differences in cost-effectiveness, as many other factors may influence the costs of HIV/AIDS interventions. It is preferable to comment on the outcomes of the interaction in terms of the observed results.

Relating the results of this study to the literature, it is noted that similar effectiveness results were obtained elsewhere. For instance, one study compared the effectiveness of treating STDs to prevent HIV transmission in a low prevalence context (Tanzania) and a relatively high prevalence one (Uganda). It was found that the treatment of STDs reduced HIV transmission to a greater degree in Tanzania than in Uganda because in the latter country HIV transmission was taking place outside the core groups with high STI rates, which were being targeted by STI interventions (Korenromp *et al.* 2005).

Despite the complexity involved in explaining the results in order to answer this study's research questions, it should be noted that there has been insufficient evidence on the CE of HIV/AIDS interventions to assist policy makers in deciding how to allocate budgets already committed to HIV/AIDS interventions. The little evidence which exists was produced internationally and was therefore aimed at international policy makers.

Consequently, the results of this study have profound policy implications. The results show policy makers that the pattern of the CE and extent of HIV/AIDS interventions are different across contexts and across interventions. These patterns of effectiveness could be used to guide the distribution of resources first across contexts according to whether or not contexts use resources efficiently and then according to how efficient an intervention is in this context relative to other contexts. Recent undertakings by the South African Government will require more resource inputs and consequently more efficient management of HIV/AIDS interventions.

Other CE studies have guided policy makers on how the next budget should be distributed across different interventions. This study suggests that improved

health outcomes might result if resources already committed were reallocated. The chapter proposes a policy based on efficiency principles that are compatible with current ethical and equity policy tenets. Since intervening in an LPC results in more health outcomes per cost and the extent is different across different types of intervention, the optimal allocation of resources in these circumstances requires the allocation of resources proportionate to the efficiency of the context and intervention.

Chapter summary

To sum up, this chapter compared the CE of HIV/AIDS interventions in an LPC and a HPC in South Africa and found that HIV/AIDS interventions were more cost-effective in an LPC. It also found that the extent of CE varied across contexts and across HIV/AIDS interventions. Policy makers should allocate resources on the basis of these CE results.

Chapter 8 : Cost-effectiveness of HIV/AIDS interventions across a rural context and an urban context

This chapter compares the CE of HIV/AIDS interventions in a rural context and an urban context. In each context, a follow-up is undertaken of the patients in an HIV/AIDS intervention and in USUAL CARE. The incremental CE ratio (ICER) of an intervention relative to USUAL CARE is calculated in each context and the ICERs of the same intervention are compared across contexts. To take account of the interaction between an HIV/AIDS intervention and the context, assumptions about the progression of patients in HIV/AIDS states are pegged to projections made by the Spectrum Policy Modelling System (SPMS). Effectiveness is measured in terms of survival and survival adjusted for the quality of life (QALYs). Sensitivity analysis is conducted on all model parameters. Section one elaborates on the methodology used; section two presents the results and section three discusses the results.

8.1 Methods

To estimate and compare the CE of an HIV/AIDS intervention across a rural context and an urban context, a Markov model for a rural context and a Markov model for the urban context are constructed for that intervention. In the absence of an HIV/AIDS intervention, patients use USUAL CARE¹⁷ and therefore a Markov model in a rural context and a Markov model in an urban context are constructed for USUAL CARE of that intervention. Each Markov model tracks a cohort of 100,000 patients in HIV/AIDS states in successive 3-month periods until all patients die. The interventions modelled are PMTCT, HAART FOR ADULTS and HAART FOR CHILDREN.

For PMTCT, patients are tracked in “uninfected”, “infected”, “AIDS” and “dead” HIV/AIDS states and those who develop AIDS are directly linked to care. It is

¹⁷ It is important to note that USUAL CARE is not a response option in the HIV/AIDS sector. However to capture the full benefits and costs of an HIV/AIDS intervention in a context, the costs and effectiveness are estimated in case patients of that intervention use USUAL CARE. USUAL CARE is therefore considered as a comparator of each of the modeled HIV/AIDS interventions and denoted with capital letters.

assumed that a cohort of 100,000 pregnancies in infected mothers starts in the “uninfected” state; within 3 months, some progress to the “infected” state, others to the “AIDS” state and still others to the “dead” state. The cohort of HIV-positive pregnant women is assumed to be on dual therapy PMTCT consisting of Zidovudine (AZT) at the 28th week of pregnancy and during labour, followed by Nevirapine (NV) for the new-born baby. The cohort is assumed to reflect HIV-positive pregnant women in South Africa for 2007 in each context. Of these women, 20% exclusively breastfeed, 62% exclusively use formula milk and 18% use mixed feeding (Soorapath *et al.*, 2006). It is assumed that in the absence of PMTCT, patients use USUAL CARE (antenatal care) in which case the Markov model tracks these patients in similar HIV/AIDS states modelled for PMTCT. The base-case Markov model structures for PMTCT and related USUAL CARE in a rural context are provided in appendices 3 and 4(pp.247-248), while the base-case Markov model structures for the same interventions in an urban context are in appendices 5 and 6 (pp.249-250)

For HAART FOR ADULTS, a cohort of 100,000 HIV infected adults starts in the “AIDS” state, that is, when their CD4 count is below 200¹⁸. In each of the successive 3-month periods, some members of the cohort remain in the HIV/AIDS state; others improve in health status to CD4 count above 200, that is, to “non-AIDS”, while the rest worsen to the “dead” HIV/AIDS state. The cohort is assumed to have the socio-economic characteristics of HIV infected adults in 2007. In the absence of HAART FOR ADULTS, patients use usual health care services in which case the Markov model tracks these patients in similar HIV/AIDS states modeled for HAART FOR ADULTS. The base-case Markov model structures for HAART FOR ADULTS and related USUAL CARE in a rural context are in appendices 7 and 8 while the base-case Markov model structures for the same interventions in an urban context are in appendices 9 and 10(pp.251-254).

For HAART FOR CHILDREN, a cohort of 100,000 HIV infected children starts in the “AIDS” state. In each of the successive 3-month periods, some members of the cohort remain in the “AIDS” state; others improve in health status to the

¹⁸ According to the South African New Treatment Guidelines, treatment starts when CD4 count falls below 350 but evidence relating to these guidelines with respect to patients’ transition probabilities and costs is not widespread. The study used evidence with treatment at CD4 200 and conducted sensitivity analysis with assumptions regarding the new treatment guidelines.

“non-AIDS” state and the rest worsen to the “dead” state. AIDS in children is defined as a stage at which there is severe illness, that is, stages 3 and 4 of the WHO guidelines (WHO, 2005). It is assumed that the cohort uses pediatric care (USUAL CARE) in the absence of HAART FOR CHILDREN in which case the Markov model tracks these patients in similar HIV/AIDS states modeled for HAART FOR CHILDREN. The cohort is assumed to have the socio-economic characteristics of HIV infected children in 2007¹⁹. The base-case Markov model structures for HAART FOR CHILDREN and USUAL CARE in a rural context are in appendices 11 and 12 while the base-case Markov model structures for the same interventions in an urban context are in appendices 13 and 14 (pp.255-258).

To estimate the costs and health outcomes of each model, the proportions of patients in HIV/AIDS states in the first 3-month period and successive 3-month periods are required. The estimation starts with determining the proportions of patients in HIV/AIDS states in the first 3-month period. These proportions are reported in Table 8:1 for PMTCT, HAART FOR ADULTS and their respective USUAL CARE.

¹⁹ It is common practice in Markov modelling to use a hypothetical cohort of patients. Since this hypothetical cohort of patients is not actually observed, its characteristics need to be assumed to be similar to the population studied. In other words the hypothetical population is assumed to be a sub-component of the population of interest. To this end, parameters collected in the population studied are applied to the hypothetical population to produce estimates of the population in question.

Table 8:1 Transition probabilities data for the base-case comparison (PMTCT, HAART FOR ADULTS and their related USUALCARE)

PMTCT	Rural context			Urban context		
Transition probability	Base – case Values (BCV)	Range	Source	Base-case values (BCV)	Range	Sources
Non-infected to infected	0.036	0.029-0.041	Goga <i>et al.</i> (2010)	0.030	(0.029-0.041)	Stover (2009)
Non-infected to death	0.18	0.10-0.25	Model derived	0.12	(0.10-0.25)	Model derived
Infected to AIDS	0.07	0.06-0.10	Goga <i>et al.</i> (2010)	0.05	(0.04-0.10)	Soorapath (2006)
Infected to death	0.06	0.06-0.10	Goga <i>et al.</i> (2010)	0.05	(0.04-0.10)	Tindyebwa <i>et al.</i> (2006)
AIDS to death	0.20	0.10-0.30	Goga <i>et al.</i> (2010)	0.13	(0.5-0.30)	Wilkinson <i>et al.</i> (2000)
USUAL CARE	Rural context			Urban context		
Transition probability	BCV	Range	Source	BCV	Range	Source
Non-infected to infected	0.33	(0.25-0.40)	Tindyebwa <i>et al.</i> (2006)	0.28	(0.25-0.50)	Tindyebwa <i>et al.</i> (2006)
Non-infected to death	0.18	(0.10-0.20)	Tindyebwa <i>et al.</i> (2006)	0.12	(0.10-0.15)	Tindyebwa <i>et al.</i> (2006)
Infected to AIDS	0.07	(0.06-0.10)	Tindyebwa <i>et al.</i> (2006)	0.05	(0.02-0.09)	Tindyebwa <i>et al.</i> (2006)
Infected to death	0.06	(0.06-0.10)	Tindyebwa <i>et al.</i> (2006)	0.05	(0.01-0.08)	Tindyebwa <i>et al.</i> (2006)
AIDS to death	0.20	(0.10-0.30)	Desmond & Boyce (2004)	0.13	(0.08-0.18)	Desmond & Boyce(2004)
HAART FOR ADULTS	Rural context			Urban context		
Transition probability	BCV	Range	Source	BCV	Range	Source
Non-AIDS to AIDS	0.01	(0.009-0.10)	Bachmann (2006)	0.001	(0.001-0.10)	Badri <i>et al.</i> (2006:67)
Non-AIDS to death	0.01	(0.001-0.10)	Cleary <i>et al.</i> (2004)	0.001	(0.001-0.10)	Badri <i>et al.</i> (2006:67)
AIDS to non-AIDS	0.10	(0.05-0.30)	Model derived	0.15	(0.05-0.30)	Model imputed
AIDS to death	0.02	(0.001-0.10)	Walensky <i>et al.</i> (2008)	0.009	(0.001-0.10)	Badri <i>et al.</i> (2006:67)
USUAL CARE	Rural context			Urban context		
Transition probability	BCV	Range	Source	BCV	Range	Source
Non-AIDS to AIDS	0		Assumption ²⁰	0		Assumption
Non-AIDS to death	0		Assumption	0		Assumption
AIDS to non-AIDS	0		Assumption	0		Assumption
AIDS to death	0.15	(0.05-0.25)	Badri <i>et al.</i> (2006)	0.12	(0.05-0.25)	Badri <i>et al.</i> (2006).

²⁰ The literature documents that in the absence of HAART, no patients who start in the AIDS state would move to the non-AIDS state. Such patients would instead see their health deteriorate (Badri *et al.*, 2006: 65). Since no patients move from AIDS to non-AIDS in USUAL CARE, no patients would transit from non-AIDS to any other HIV state. In the absence of transition probabilities for South Africa, African evidence such as in Tindyebwa *et al.* (2006) was used. Using evidence from other studies in situations comparable to the situation of a specific study is a norm in cost-effectiveness analysis. For instance, Walensky *et al.* (2011:29-30) and Backman (2006) used some parameters from Africa and Cote d'Ivoire in estimating the CE of VCT and HAART in South Africa, respectively.

Similarly, the proportions of patients in HIV/AIDS states in the first 3-month period are reported for HAART FOR CHILDREN. These data are reported in Table 8.2.

Table 8:2 Transition probabilities data for the base-case comparison (HAART FOR CHILDREN and related USUAL CARE)

HAART FOR CHILDREN	Rural context			Urban context		
	values	Range	source	Value	Range	Sources
Non-AIDS to AIDS	0.01	(0.009-0.10)	Bachmann (2006)	0.001	(0.001-0.10)	Badri <i>et al.</i> (2006:67)
Non-AIDS to death	0.01	(0.001-0.10)	Cleary <i>et al.</i> (2004)	0.001	(0.001-0.10)	Badri <i>et al.</i> (2006:67)
AIDS to non-AIDS	0.10	(0.05-0.30)	Model derived	0.15	(0.05-0.30)	Model imputed
AIDS to death	0.02	(0.001-0.10)	Walensky <i>et al.</i> (2008)	0.009	(0.001-0.10)	Badri <i>et al.</i> (2006:67)
USUAL CARE	Rural context			Urban context		
	Value	Range	Sources	Value s	range	Sources
Non-AIDS to AIDS	0		Assumption ²¹	0		Assumption
Non-AIDS to death	0		Assumption	0		Assumption
AIDS to non-AIDS	0		Assumption	0		Assumption
AIDS to death	0.15	(0.05-0.25)	Badri <i>et al.</i> (2006)	0.12	(0.05-0.25)	Cleary <i>et al.</i> (2006)

The proportion of patients in HIV/AIDS states in subsequent 3-month periods is assumed on the basis of trends observed in SPMS projections. This assumption is based on the fact that these projections are done using parameters collected in these contexts. Therefore, the costs and effectiveness estimates based on SPMS projection trends are obtained taking into account the interaction between the intervention and the context. In each context, SPMS projections depict such interactions. The proportion of patients who become infected or die in the next period is determined by adjusting the proportion in the current period according to the proportion infected or dying as per SPMS projections. Appendix 15 on p.259 explains how this adjustment is done in low and high HIV prevalence contexts; these adjustment procedures are similar to the adjustment procedures used in this chapter with the only difference being that, in this chapter, the adjustments are based on the projections of SPMS.

²¹ The literature documents that in the absence of HAART, no patients who start in the HIV/AIDS state would move to the Non-aid state. Such patients would instead see their health deteriorate (Badri *et al.*, 2006: 65). Since no patients move from AIDS to non-AIDS in USUAL CARE, no patients would transit from non-AIDS to any other HIV/AIDS state.

The cost applied to patients in various HIV/AIDS states is based on the evidence collected from the literature for the first 3-month period. This cost is assumed to be constant over time. Cost has been found to decrease further into the intervention, due to increased experience or economies of scale (Menzies *et al.*, 2012). The decrease in unit cost over time is not considered in the present analysis given its insignificant effect on the results observed from the previous analysis in Chapter 7. Unit costs are adjusted to reflect either the societal or government perspective. Estimates of unit costs for transport and waiting time in public sector facilities are used to estimate costs from the point of view of society. The costs are measured in constant 2007 US\$ and discounted at 3% for the base-case comparison. Table 8:3 provides the evidence of cost measured from the government perspective.

Table 8:3 Three-month cost data for the base-case comparison (government perspective)

PMTCT intervention				
	Rural context		Urban context	
HIV/AIDS states	Base-case value	Source	Value	Sources
Non-infected	\$200(100-300)	Pelitzer <i>et al.</i> (2006)	250 (100-300)	Hussain <i>et al.</i> (2011)
Infected	\$200 (100-300)	Desmond & Boyce (2004)	250 (100-300)	Hussain <i>et al.</i> (2011)
AIDS	\$350(100-300)	Desmond & Boyce (2004)	400 (200-500)	Meyers <i>et al.</i> (2007)
Death	\$50 (0-100)	Case <i>et al.</i> (2008)	75 (0-100)	Case <i>et al.</i> (2008)
USUAL CARE				
HIV/AIDS state	Value	Source	Value	Sources
Non-infected	\$200(100-300)	Hoque <i>et al.</i> (2008)	250 (100-300)	Tshabalala (2012)
Infected	\$200(100-300)	Hoque <i>et al.</i> (2008)	250 (100-300)	Sibeko & Moodley (2006)
AIDS	\$375(100-300)	Clealry <i>et al.</i> (2006)	425 (200-500)	Badri <i>et al.</i> (2006)
Death	\$50 (0-100)	Case <i>et al.</i> (2008)	75 (0-100)	Meyer-Rath <i>et al.</i> (2012)

Note: The cost in "death" was considered as once-off cost in the estimation of the cost for the cohort.

The quality of life data in the rural context is assumed to be lower in the rural context than it is in the urban context in each HIV/AIDS state except the "dead" state. This assumption is based on the fact that a rural context abounds with circumstances which aggravate the health status of patients. It is based on the quality of life estimates which have been produced in the country (Jelsma *et al.*, 2005); O'Keefe & Wood, 1996; Louwagie *et al.*, 2007). In each context, the quality of life in USUAL CARE is assumed to be lower (details in appendix 20 on p.267). The base-case values of the quality of life data used in the analysis are in Table 8.4.

Table 8:4 Quality of life data used in an intervention

HIV state	Rural context		Urban context	
PMTCT	Base case value (BCV)	Evidence base	Base case Value (BCV)	Evidence base
Non-infected Infected with no AIDS AIDS Deaths	0.90 0.67 0.30 0	Jelsma <i>et al.</i> (2006), O’Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O’Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O’Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O’Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007)	0.95 0.75 0.65 0	Jelsma <i>et al.</i> (2006) & O’Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O’Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O’Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O’Keeffe & Wood (1996)
HAART FOR ADULTS	BCV	Evidence base	BCV	Evidence base
Non-AIDS AIDS Deaths	0.67 0.55 0	Jelsma <i>et al.</i> (2006), O’Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O’Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O’Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007)	0.90 0.70 0	Jelsma <i>et al.</i> (2006) & O’Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O’Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O’Keeffe & Wood (1996)
HAART FOR CHILDREN	BCV	Evidence base	BCV	Evidence base
Non-AIDS AIDS Death	0.67 0.50 0	Jelsma <i>et al.</i> (2006), O’Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O’Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007) Jelsma <i>et al.</i> (2006), O’Keeffe & Wood (1996), Louwagie <i>et al.</i> (2007)	0.80 0.70 0	Jelsma <i>et al.</i> (2006) & O’Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O’Keeffe & Wood (1996) Jelsma <i>et al.</i> (2006) & O’Keeffe & Wood (1996)

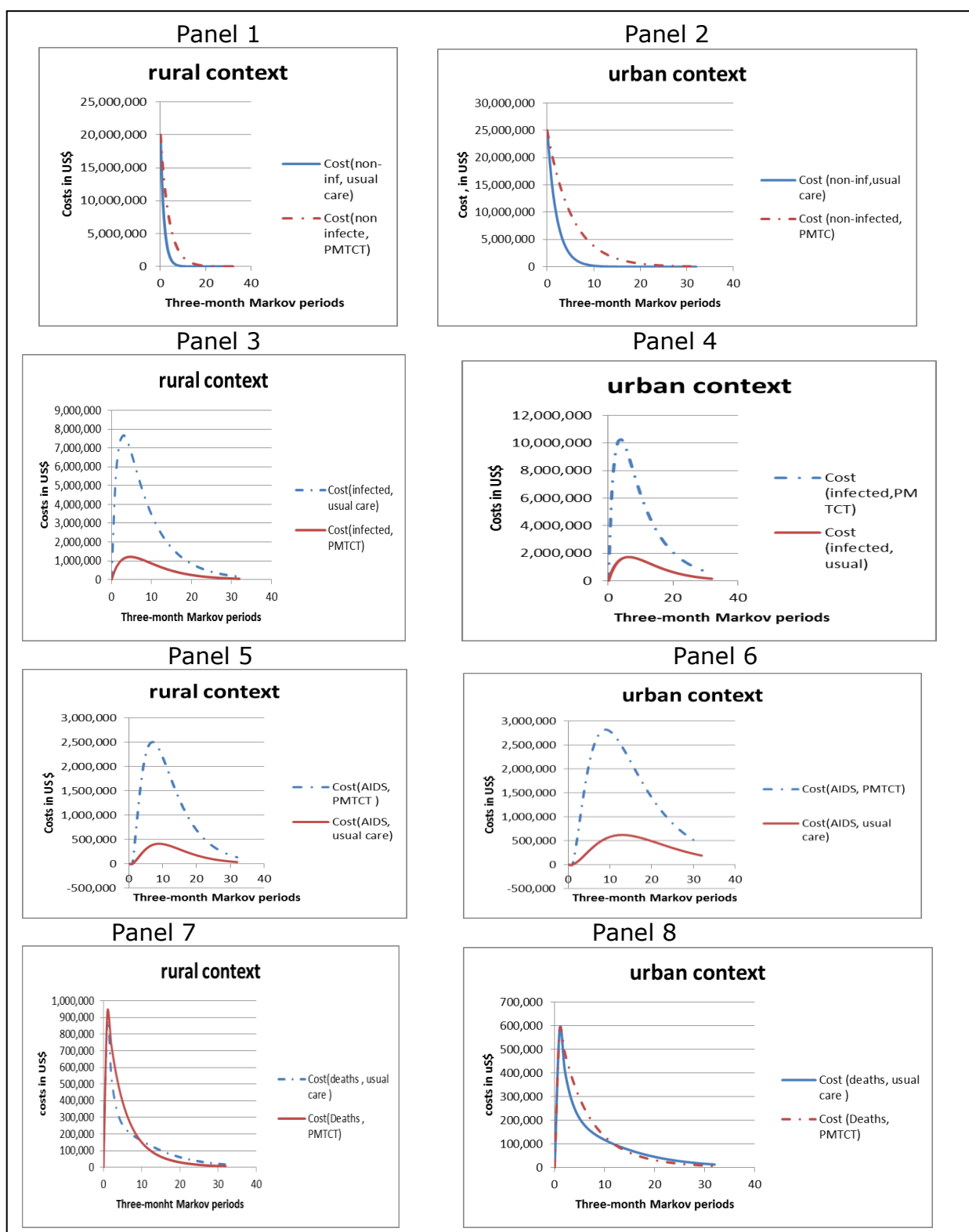
Note:

8.2 Results

This section presents the results. It provides a detailed comparison of the costs of a given intervention in HIV/AIDS states across contexts; makes similar comparisons for effectiveness; compares the CE of the base-case analysis and conducts sensitivity analysis.

8.2.1 Costs

An understanding of how the CE of an HIV/AIDS intervention compares across a rural context and an urban context requires a separate analysis of the cost and effectiveness of that intervention. In this section, the analysis of cost is done by assessing additional cost, in each HIV/AIDS state, of an HIV/AIDS intervention relative to the costs of USUAL CARE. Figure 8:1 compares the additional cost of PMTCT with the cost of USUAL CARE for different HIV/AIDS states across a rural context and an urban context.



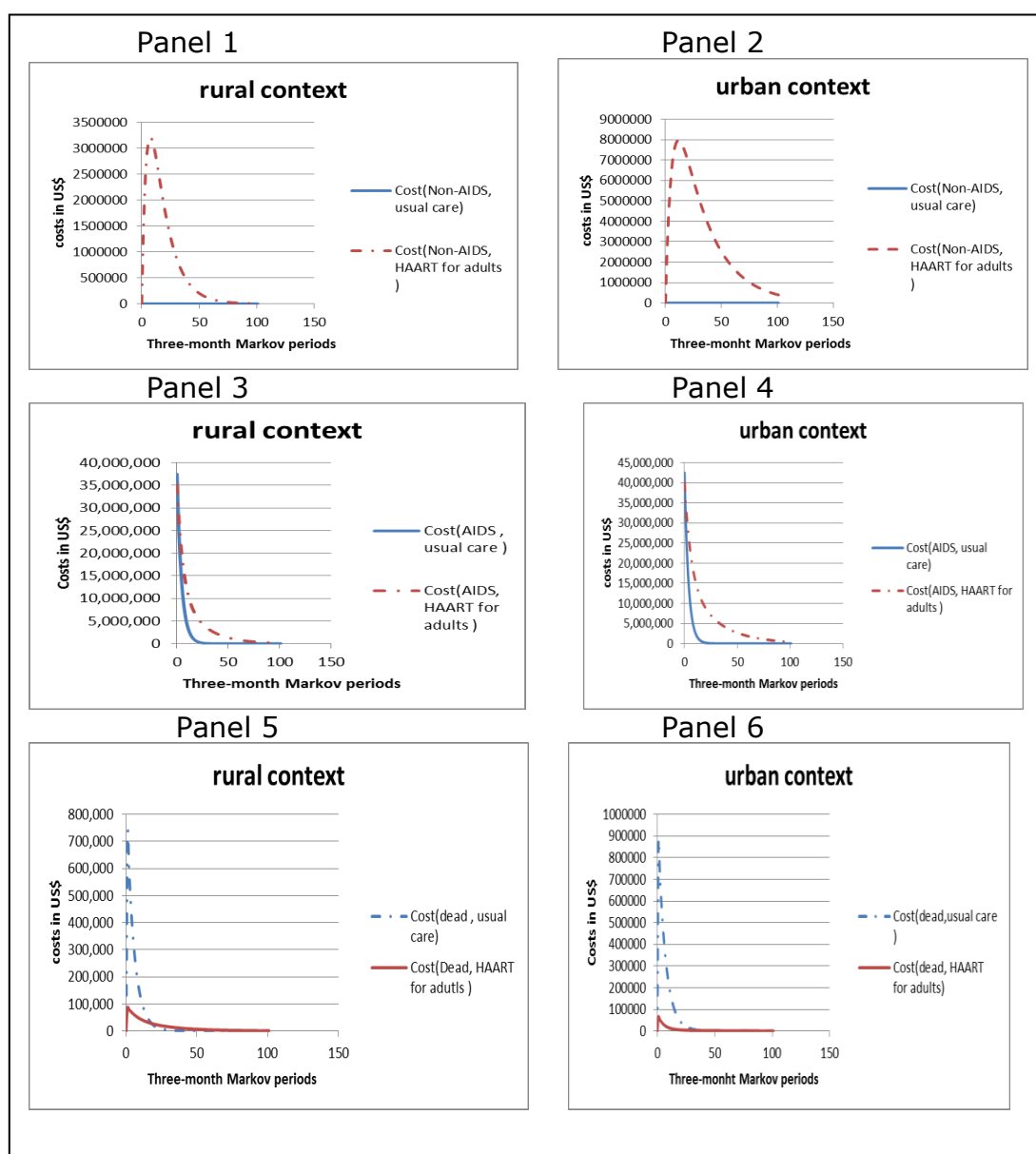
Source: Author, based on the results of Markov models' simulations.

Figure 8:1 Comparison of lifetime cost of PMTCT across a rural context and an urban context (in US\$, government perspective)

As Figure 8:1 shows, the cost of USUAL CARE is clearly less than the cost of PMTCT. However, how the areas between the PMTCT "infected" curves and

USUAL CARE “infected” curves compared across a rural and an urban context are not clear. Graphically, these curves appear to be similar (see Panel 3 and Panel 4).

In HAART FOR ADULTS however, the pattern of costs is somewhat different. Figure 8:2 show these results.



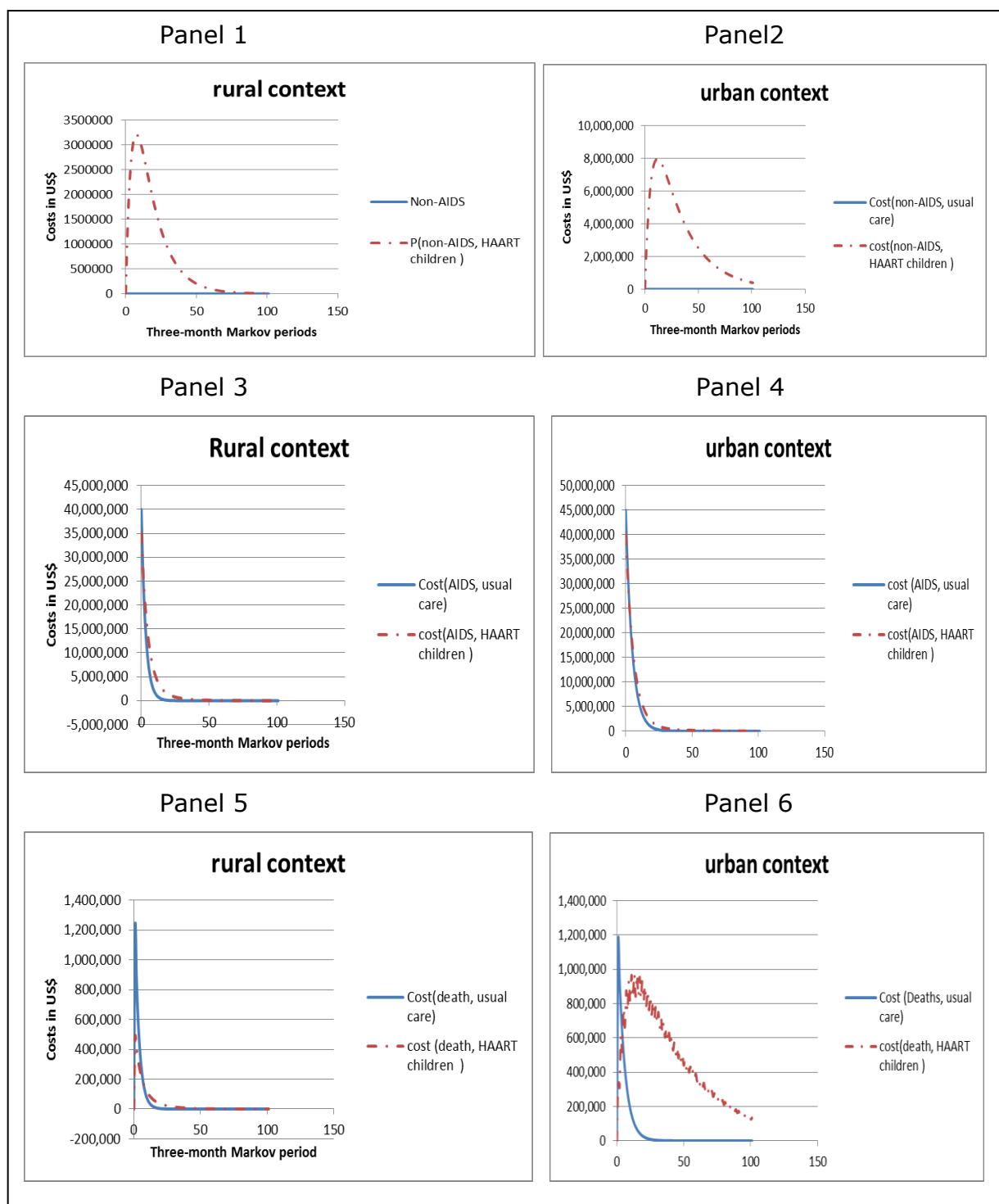
Source: Author, based on the results of Markov models' simulations.

Figure 8:2 Comparison of lifetime costs of HAART FOR ADULTS across a rural context and an urban context (in US\$, government perspective)

Figure 8:2 indicates that the cost of USUAL CARE is lower than the cost of HAART FOR ADULTS regardless of HIV/AIDS state considered. The figure also

shows that the difference between the cost curves of HAART FOR ADULTS and the cost curves of USUAL CARE is greater in an urban context than it is in a rural context for all HIV/AIDS states, at least on the basis of difference in scale (Panel 1 to Panel 6). This result indicates that HAART FOR ADULTS is more costly in an urban context than in a rural context.

In HAART FOR CHILDREN, the costs of HAART are also greater than the cost of USUAL CARE. Figure 8:3 shows the results.



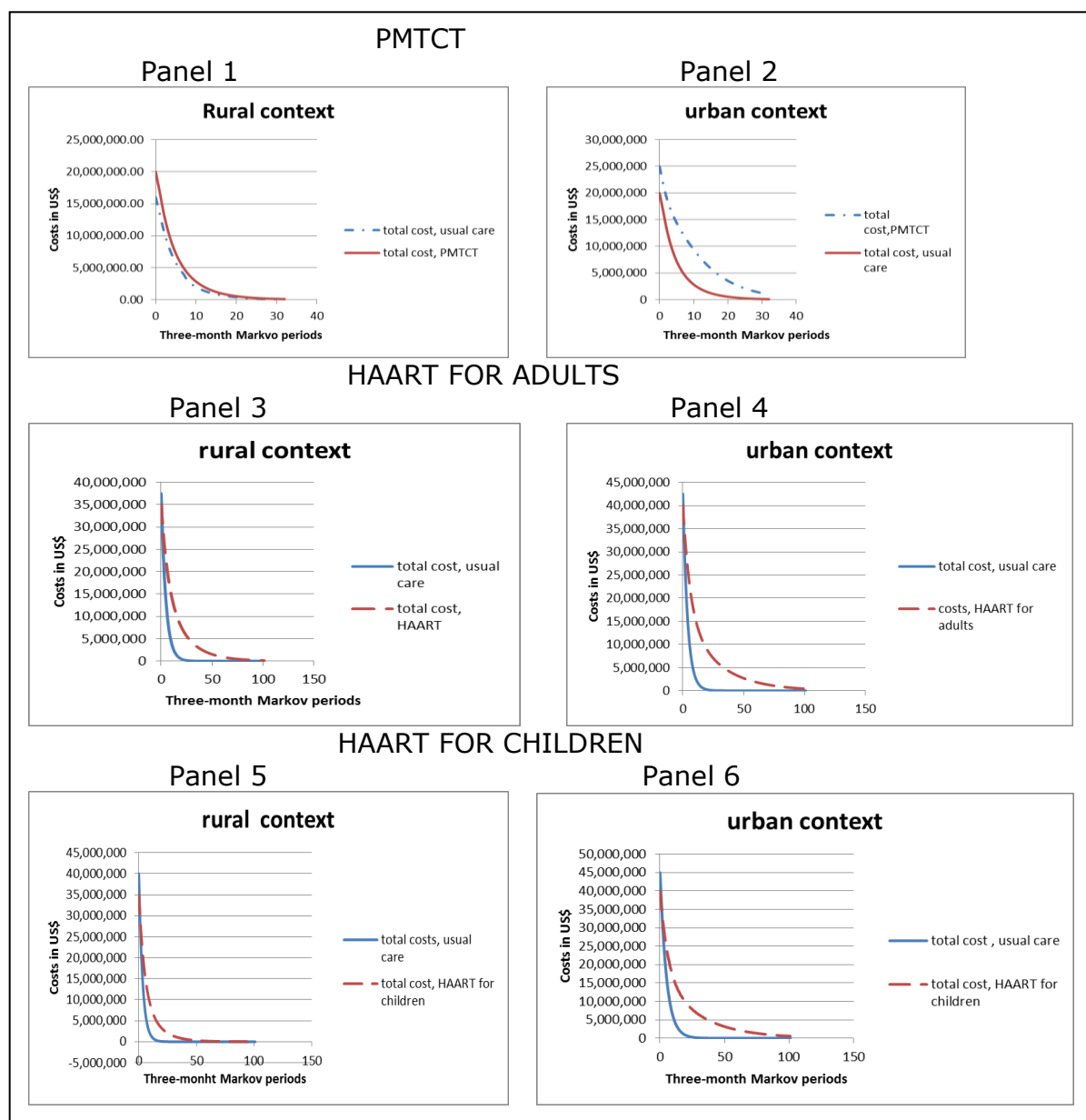
Source: Author, based on the results of Markov models' simulations.

Figure 8:3 Comparison of lifetime costs of HAART FOR CHILDREN across a rural context and an urban context (in US\$, government perspective)

The areas between the cost curve of HAART for Children and that of USUAL CARE are greater for the urban context; this holds for HIV/AIDS states "non-AIDS" and "dead". This result indicates that, relative to USUAL CARE, HAART for

CHILDREN is more costly in the urban context than it is in the rural context except in the “AIDS” state where differences are not graphically clear (Panel 3 and Panel 4) indicating that there is no difference in this state.

Analysing the overall costs rather than the costs in each in HIV/AIDS state allows for an overall assessment of how the costs of HIV/AIDS interventions compare across contexts. These results are shown in Figure 8:4.



Source: Author, based on the results of Markov models' simulations.

Figure 8:4 Comparison of the lifetime overall cost of HIV/AIDS interventions across a rural context and an urban context (in US\$, government perspective)

As the results in Figure 8:4 suggest, the difference between the costs of PMTCT relative to the cost of USUAL CARE in the rural context is much lower than the difference between the costs of PMTCT relative to the cost of USUAL CARE in the urban context (Panel 1 to 6). This result implies that PMTCT costs more in the urban context than it does in the rural context because of the inherent factors in each context that cannot be identified given the context of the study.

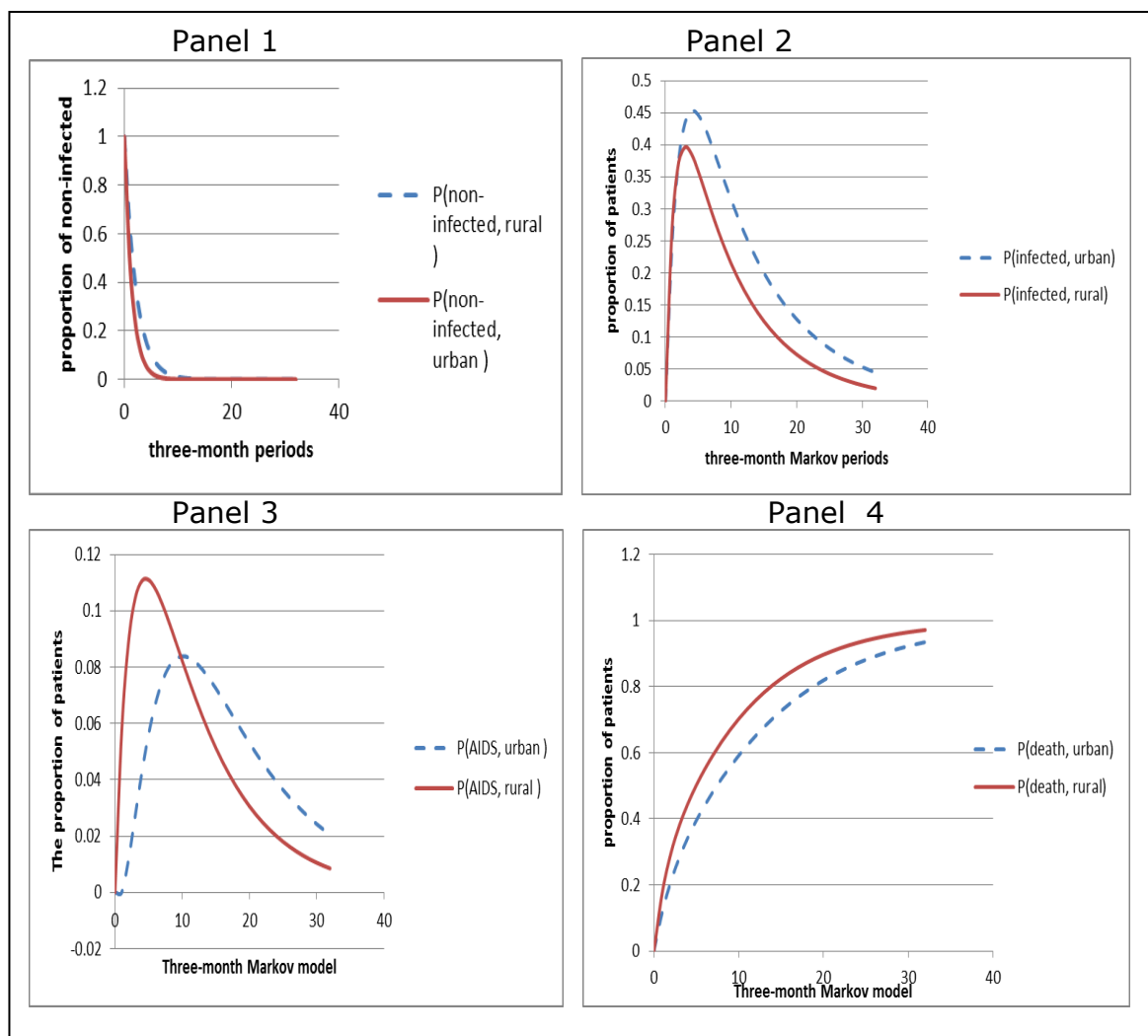
The cost of HAART FOR ADULTS, relative to the cost of USUAL CARE, is also greater in the urban context than in the rural context. This also applies to HAART FOR CHILDREN. The next section discusses the effectiveness of HIV/AIDS interventions.

8.2.2 Effectiveness

This section compares the effectiveness of HIV/AIDS interventions across rural and urban contexts. It reports different types of comparisons across a rural and an urban context, notably: comparison of survival in the case of USUAL CARE; comparison of additional survival in terms of an HIV/AIDS intervention; comparison of life-years gained by an HIV/AIDS intervention; and comparison of QALYs (life-years adjusted with the quality of life) gained by an HIV/AIDS intervention.

8.2.2.1 Comparisons of survival across a rural context and an urban context: USUAL CARE

To grasp the extent to which the effectiveness of an HIV/AIDS intervention might differ across a rural context and an urban context, the analysis starts by comparing survival patterns across these two contexts in the case of USUAL CARE, that is, in the absence of any HIV/AIDS intervention. Figure 8:5 shows survival patterns across a rural and an urban context in the absence of PMTCT.

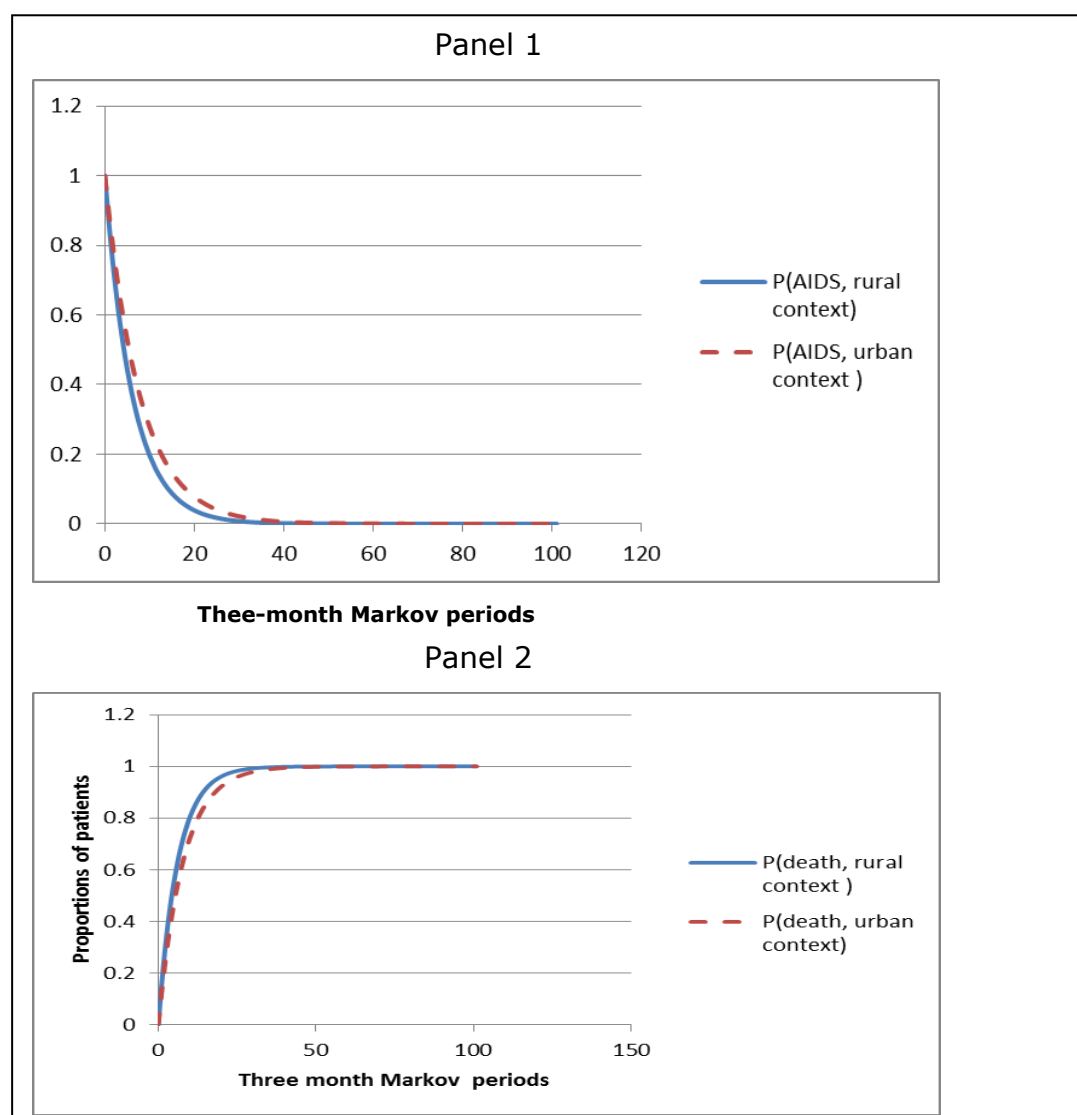


Source: Author, based on the results of Markov models' simulations

Figure 8:5 Comparison of survival patterns across a rural context and an urban context in the absence of PMTCT

Figure 8:5 shows that over time the proportions of cohorts in various HIV/AIDS states are not the same in a rural context as in an urban context despite an assumption that patients in each context start in the "non-infected" state. Panel 1 of Figure 8:5 shows that over time, a rural context shows greater proportions of patients in the "non-infected" state than an urban context. This result conforms to the results in Panel 2 of the figure which show that, over time, an urban context shows greater proportions of patients in the "infected" state. While greater proportions of those in the "infected" state in the urban context seems to suggest worse health outcomes in the urban context, Panel 3 and Panel 4 of the figure show that the rural context accounts for greater proportions of patients in worse HIV/AIDS states, notably "AIDS" and "deaths". This result suggests that even though greater proportions of patients succumb to infections in the urban context, an even greater proportion among those infected in the

rural context succumb to worse HIV/AIDS, states notably “AIDS” and “deaths”. The reason is that living conditions in the rural contexts are likely to propel the infected into these worse states. This gap could be narrowed by intervening in rural areas to improve living conditions, such as providing better nutrition. Figure 8:6 compares survival patterns across rural and urban contexts in the absence of HAART FOR ADULTS.

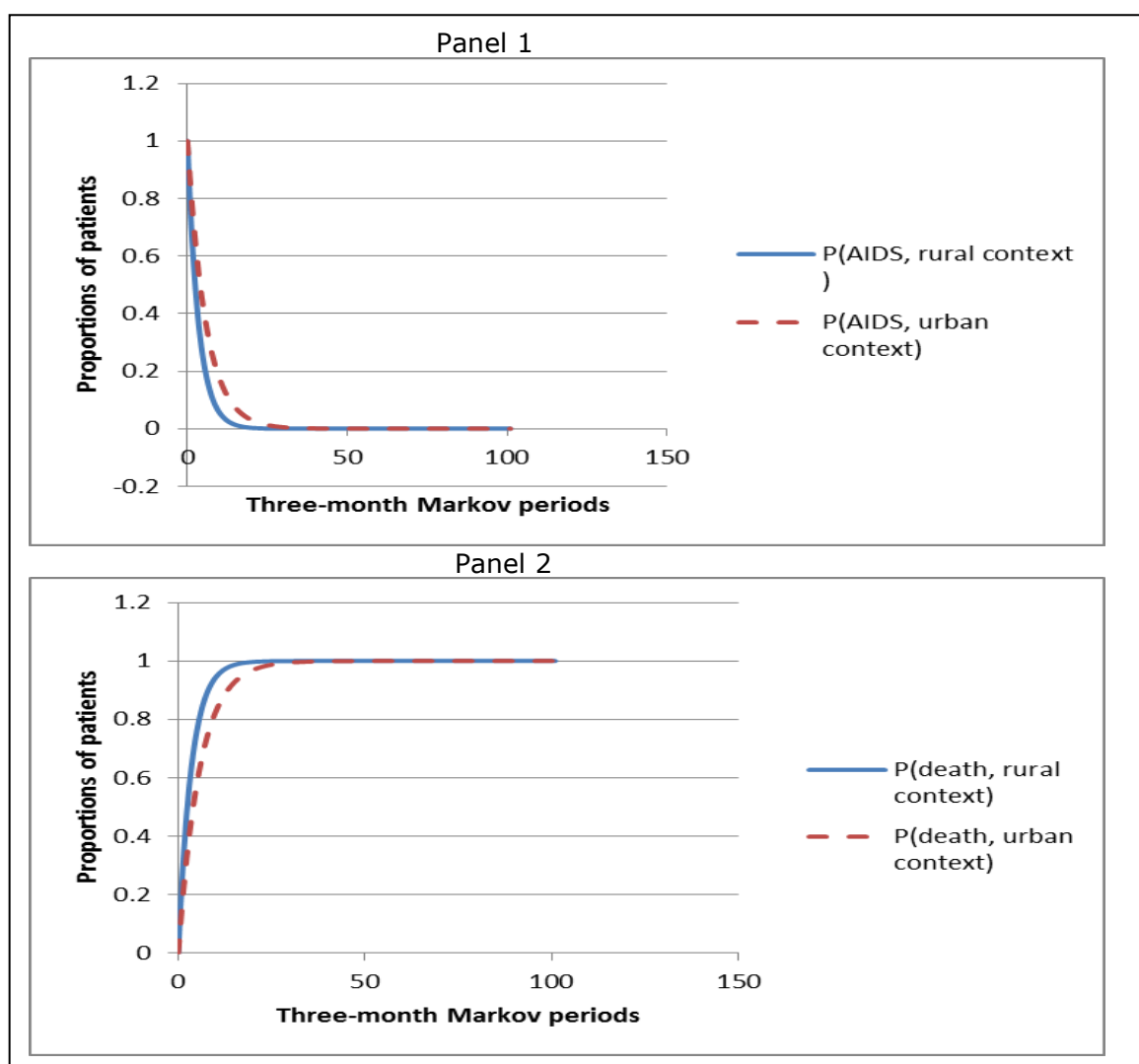


Source: Author, based on the results of Markov models' simulations.

Figure 8:6 Comparison of survival patterns across a rural context and urban context in the absence of HAART FOR ADULTS

As Figure 8:6 shows, greater proportions of patients are in better HIV/AIDS states in the urban context than they are in the rural context. The Figure shows that greater proportions of patients are in the “AIDS” state in the urban context than in the rural context (Panel 1), while more patients are in the “dead” state in

the rural context than in the urban context (Panel 2). This result implies that there are fewer patients in severe HIV/AIDS states in the urban context than in the rural context due to poor living conditions in the latter context. It is worth noting that in the case of USUAL CARE, no patients are found in “non-AIDS” states. In fact, since all patients starts in AIDS states, one would not expect any improvement in the health of AIDS patients without HAART FOR ADULTS. The same survival patterns across these contexts apply to HAART FOR CHILDREN who use USUAL CARE, as shown in Figure 8:7.



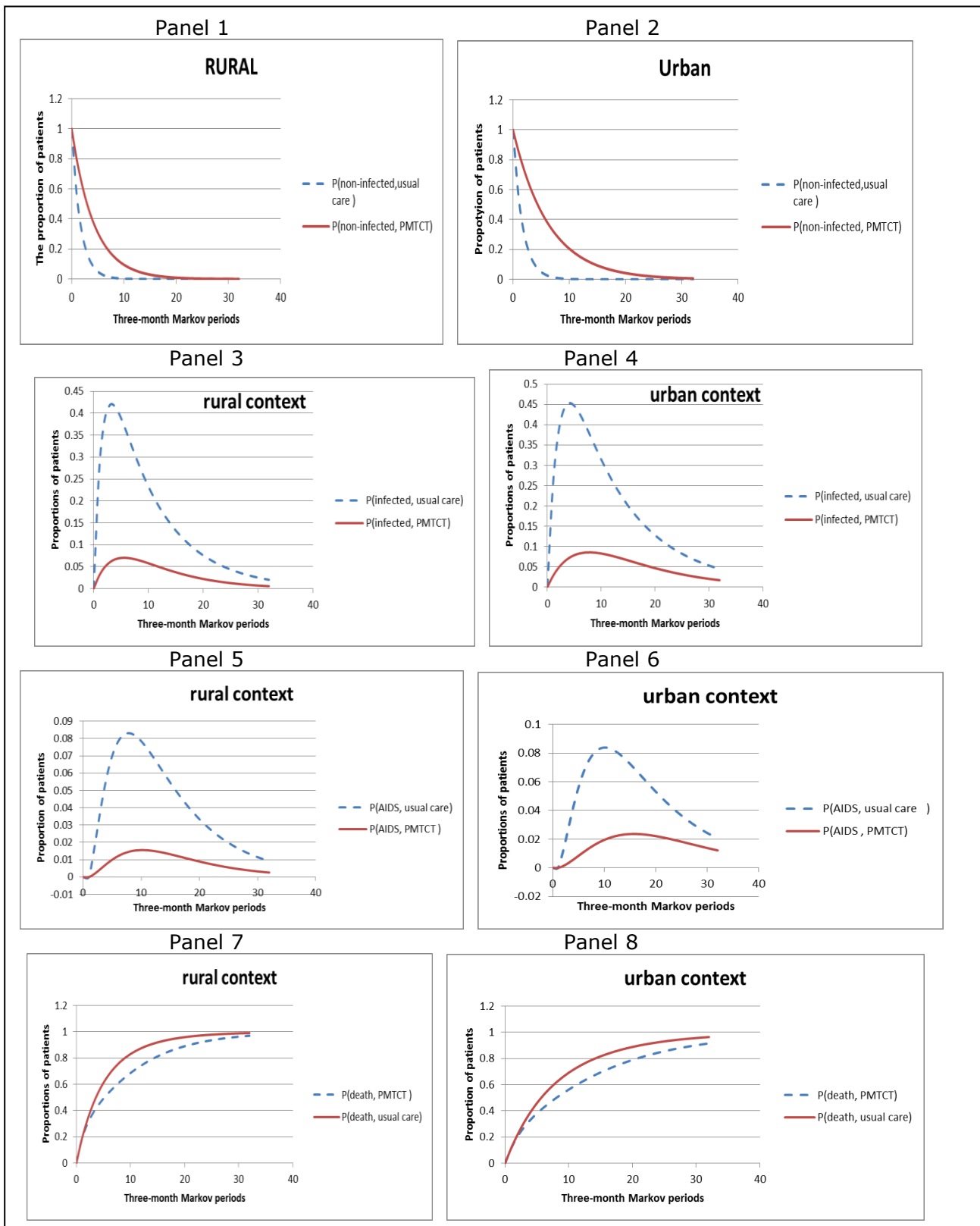
Source: Author, based on the results of Markov models' simulations.

Figure 8:7 Comparison of survival patterns across a rural context and an urban context in the absence of HAART FOR CHILDREN

Again, it is noted in Figure 8:7 that the “AIDS” state accounts for greater proportions of patients in the urban context than the rural context (Panel 1). However, the opposite is true for the “dead” state, which accounts for greater proportions of patients in the rural context (Panel 2). Given that all patients start in the “AIDS” state, greater proportions of patients in the “dead” state in the rural context suggest worse survival patterns in the rural context due to more adverse contextual factors in the latter context.

8.2.2.2 Comparisons of additional survival across a rural context and an urban context of an HIV/AIDS intervention

The above results have shown that rural/urban contexts have an impact on survival patterns even in the absence of HIV/AIDS interventions. To take the impact of contexts into account, the additional survival of an HIV/AIDS intervention relative to the survival of USUAL CARE in a rural context, is compared with the additional survival of that intervention relative to the survival of USUAL CARE in an urban context. These results are provided in Figure 8:8 for PMTCT.

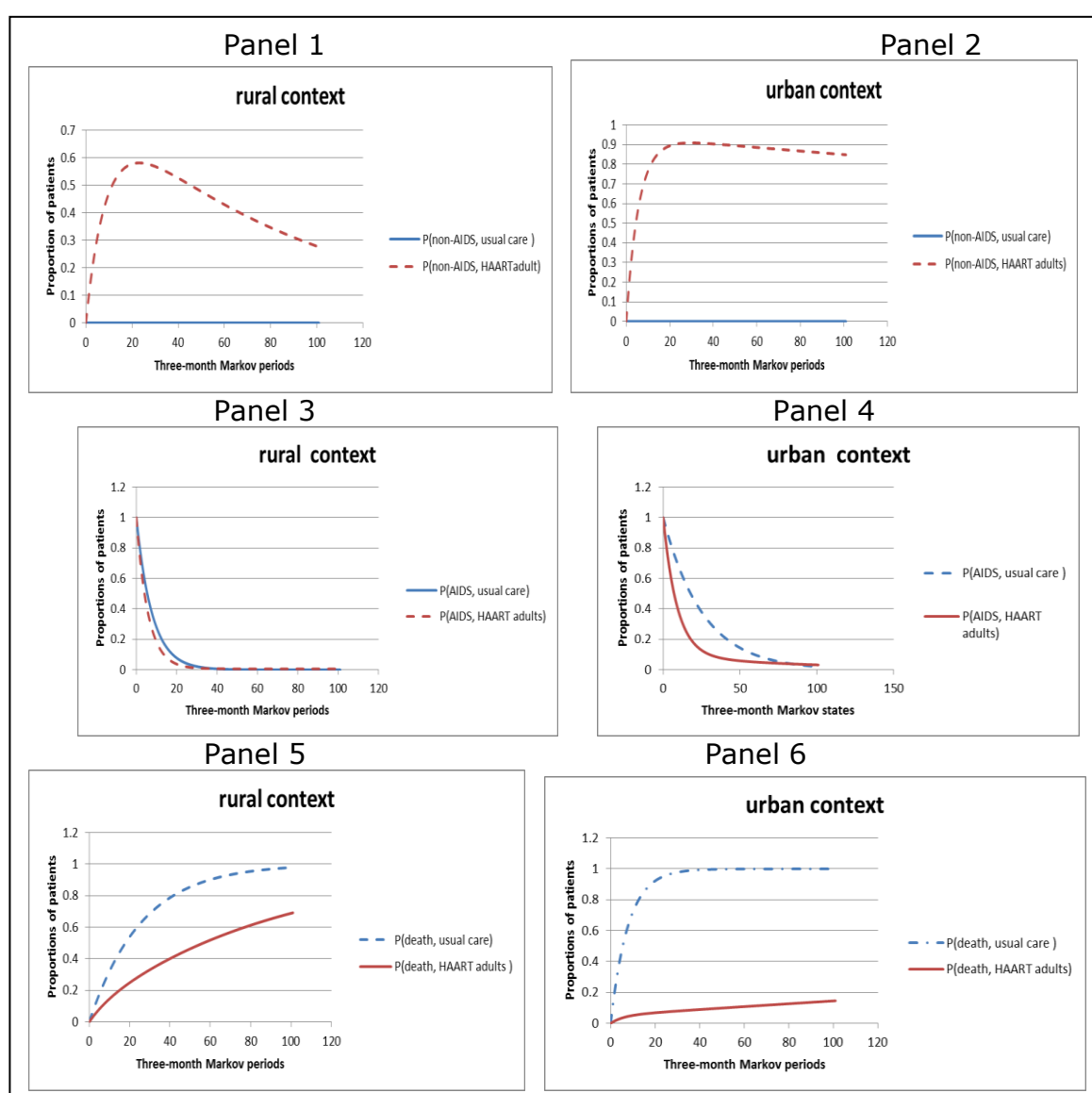


Source: Author, based on the results of Markov models' simulations.

Figure 8:8 Comparison of effectiveness of PMTCT and USUAL CARE across a rural context and an urban context

Figure 8:8 shows that survival in HIV/AIDS state curves for USUAL CARE and PMTCT are different in each context. Furthermore, the height between the survival in HIV/AIDS state curves for USUAL CARE and survival in HIV/AIDS curves for PMTCT are generally greater in the urban context than in the rural context (see comparisons shown by Panel 1 and Panel 2, Panel 3 and Panel 4, Panel 5 and Panel 6).

In HAART FOR ADULTS, the difference in effectiveness across a rural context and an urban context is clearer. Figure 8:9 shows these results.



Source: Author, based on the results of Markov models' simulations.

Figure 8:9 Comparison of effectiveness of HAART FOR ADULTS and USUAL CARE across a rural context and an urban context

Figure 8:9 clearly demonstrates the effectiveness of HAART relative to USUAL CARE in an urban or a rural context. The first two panels (Panel 1 and Panel 2) of the figure show the HAART FOR ADULTS “non-AIDS” curve and USUAL CARE “non-AIDS” curve in each context. The panels show that the USUAL CARE “non-AIDS” curve is on the horizontal axis in each context, indicating that none of the patients who start in the “AIDS” state in USUAL CARE transit to the “non-AIDS” state.

In contrast, positive proportions of patients who have access to HAART FOR ADULTS transit to the “non-AIDS” state in each context as shown in Panel 1 and Panel 2. These panels show further that, relatively more patients in the urban context transit to this state. This result is shown by a greater gap between the HAART “non-AIDS” curve and the USUAL CARE “non-AIDS” curve in the urban context (Panel 1 and Panel 2). The result provides evidence of the greater effectiveness of HAART FOR ADULTS in an urban context than in a rural context for this HIV/AIDS state.

This pattern of results applies to “AIDS” (Panel 3 and Panel 4) and “death” states (Panel 5 and Panel 6). The figure shows that the gap between the HAART FOR ADULTS “AIDS” curve and USUAL CARE “AIDS” curve is greater in the urban context than it is in the rural context (Panel 3 and Panel 4). Since the HAART FOR ADULTS curve is below the USUAL CARE AIDS curve in each context, the greater gap in the urban context implies that HAART reduces AIDS more in the urban context than it does in the rural context. Similarly, since in each context the HAART FOR ADULTS “death” curve is below the USUAL CARE “death” curve, the greater gap between the curves (Panel 5 and Panel 6) in the urban context implies that HAART reduces more deaths in the urban context than it does in the rural context.

Briefly, these results demonstrate that HAART FOR ADULTS is more effective in the urban context than in the rural context. Some of the reasons could be that the rural context experiences adverse factors such as poor nutrition, a lack of access to basic sanitation, stigma that prevents people from accessing interventions and many other adverse factors that are worse in this context than

the urban context. The patterns of the results for HAART FOR ADULTS are similar to the results for HAART FOR CHILDREN, presented in Figure 8:10.

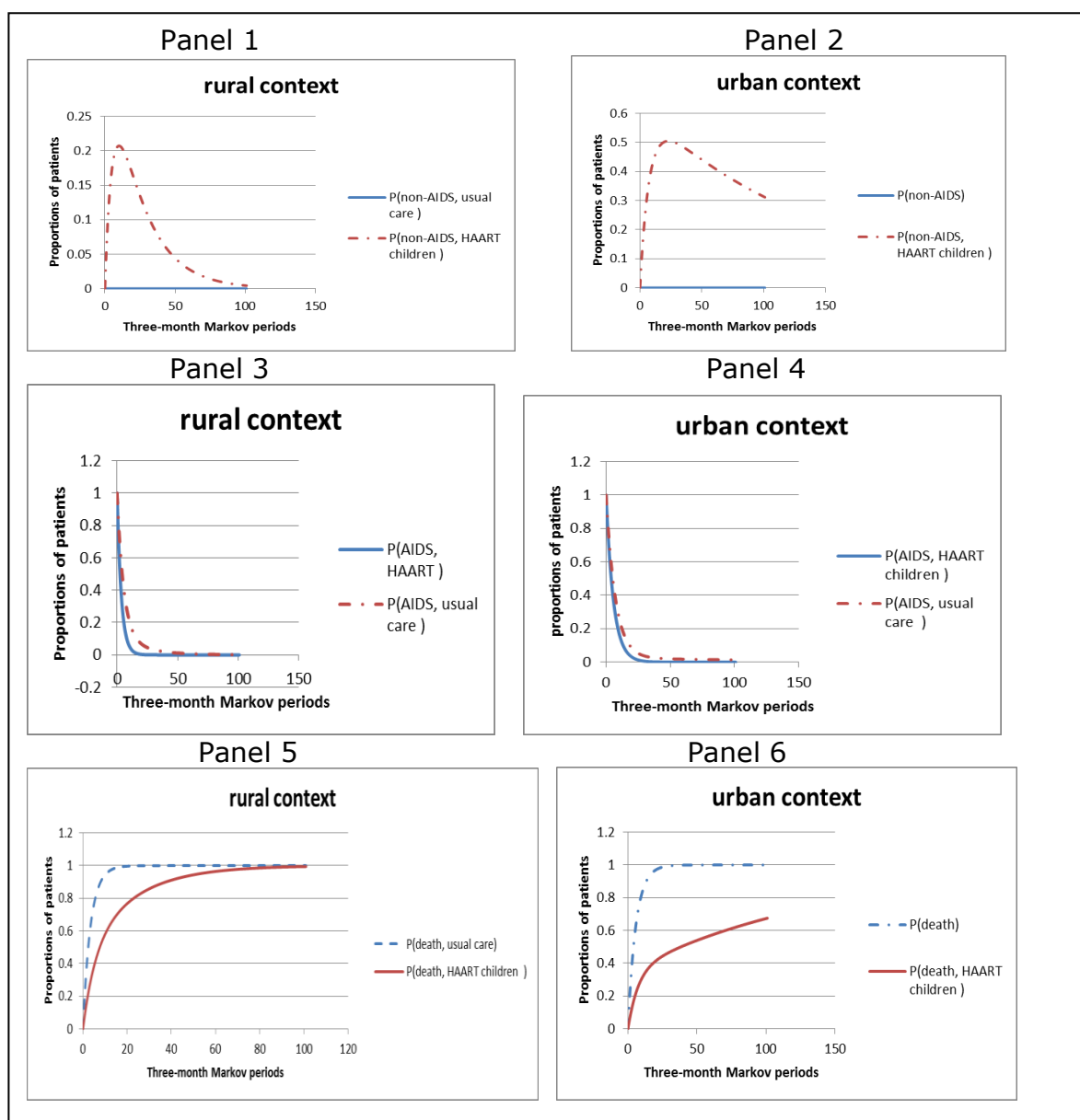
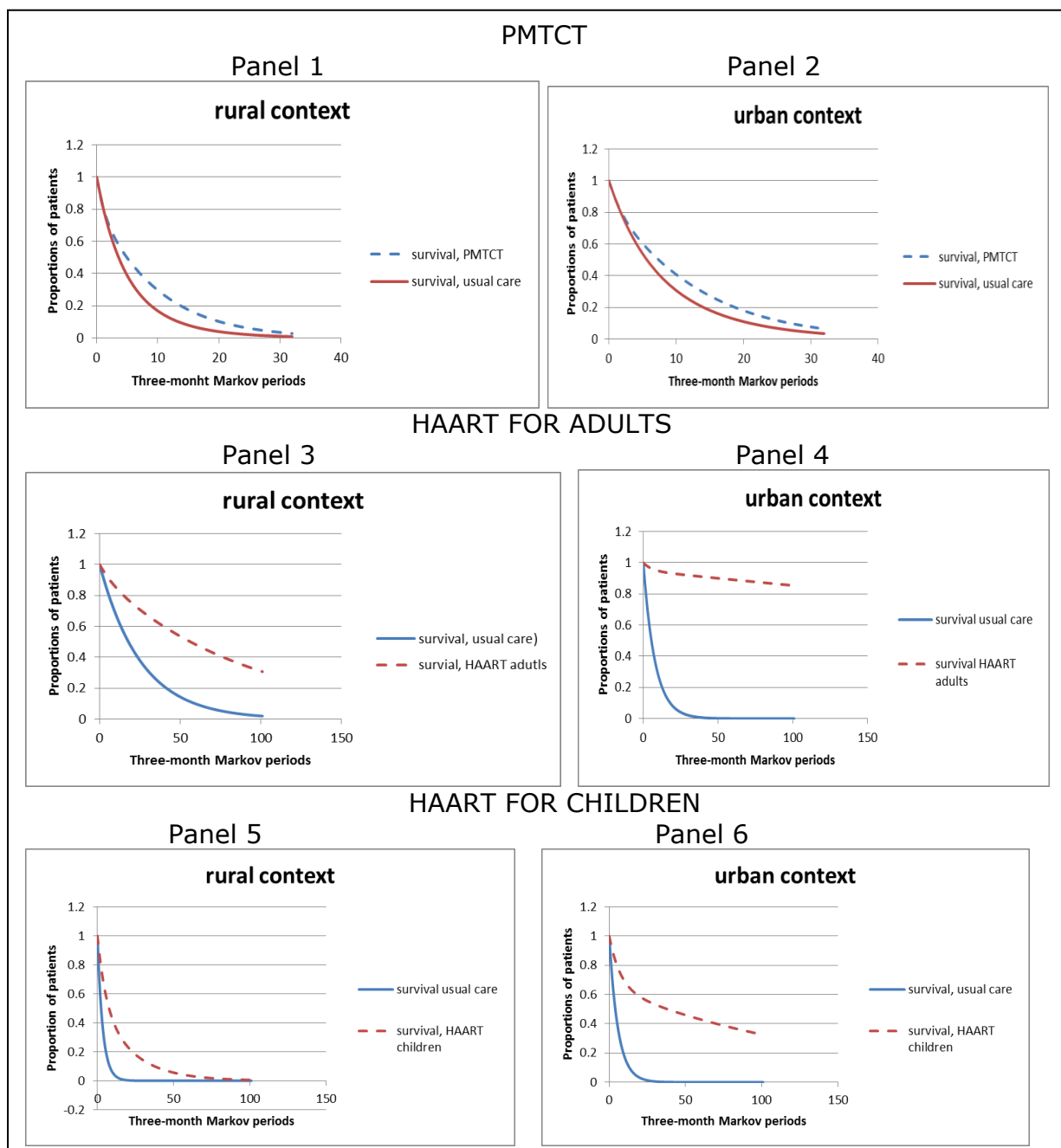


Figure 8:10 Comparison of effectiveness of HAART FOR CHILDREN and USUAL CARE across a rural context and an urban context

As in previous analysis, HAART FOR CHILDREN results in positive proportions of patients moving to the "non-AIDS" state from the "AIDS" state, while USUAL CARE results in no one moving to the "non-AIDS" state. Figure 8:10, Panel 1 and Panel 2 shows that the HAART FOR CHILDREN "non-AIDS" curve is above the USUAL CARE "non-AIDS" curve in each context. The fact that the gap between the two curves is greater in the urban context than in the rural context (Panel 1 and Panel 2) implies that HAART FOR CHILDREN causes more children

to transit to the “non-AIDS” state in the urban context than it does in the rural context, suggesting greater effectiveness of this intervention in an urban context. However, the gap between the HAART FOR CHILDREN “AIDS” curve and USUAL CARE “AIDS” curve is greater in the rural context than in the urban context (Panel 3 and Panel 4). A comparison of the data in Panel 5 and Panel 6, suggests that HAART FOR CHILDREN reduces more deaths in an urban context than it does in a rural context. Figure 8:11 compares the overall effectiveness of HIV/AIDS interventions relative to USUAL CARE.



Source: Author, based on the results of Markov models' simulations.

Figure 8:11 Comparison of overall effectiveness (survival) of HIV/AIDS interventions across a rural context and an urban context

Figure 8:11 indicates that relative to USUAL CARE, all interventions are not equally effective across rural/urban contexts. The results suggest that PMTCT is relatively more effective in the rural context on the basis of the gap between the PMTCT survival curve and the USUAL CARE survival curve, although the difference in the gap across contexts is not substantial (Panel 1 and panel 2). While the gap between the PMTCT and USUAL CARE curves across a rural and an urban context is almost insignificant, the gap is significant with HAART FOR

ADULTS and HAART FOR CHILDREN (Panel 3 and Panel 4, Panel 5 and Panel 6). The reason for this may be that children in advanced stages of HIV/AIDS may not respond to HIV/AIDS treatment as well as adults. The results show that HAART FOR ADULTS and HAART FOR CHILDREN are relatively more effective in an urban context than they are in a rural context on the basis of the gap between the survival curves for the two interventions and the USUAL CARE curves. The fact that the gap is greater in the urban context than it is in the rural context means that these interventions are more effective in an urban context. This is probably due to the existence of welfare services in the urban context which cushion the impact of HIV/AIDS.

8.2.2.3 Comparisons of life-years gained by an HIV/AIDS intervention across a rural context and an urban context

The life-years gained by an intervention are an important measure of effectiveness. To estimate life-years in each Markov period, the cohort of patients is multiplied by the proportion of patients in an HIV/AIDS state and the number of years the cohort spent in this state, 0.25, since three months is 25% of a year.

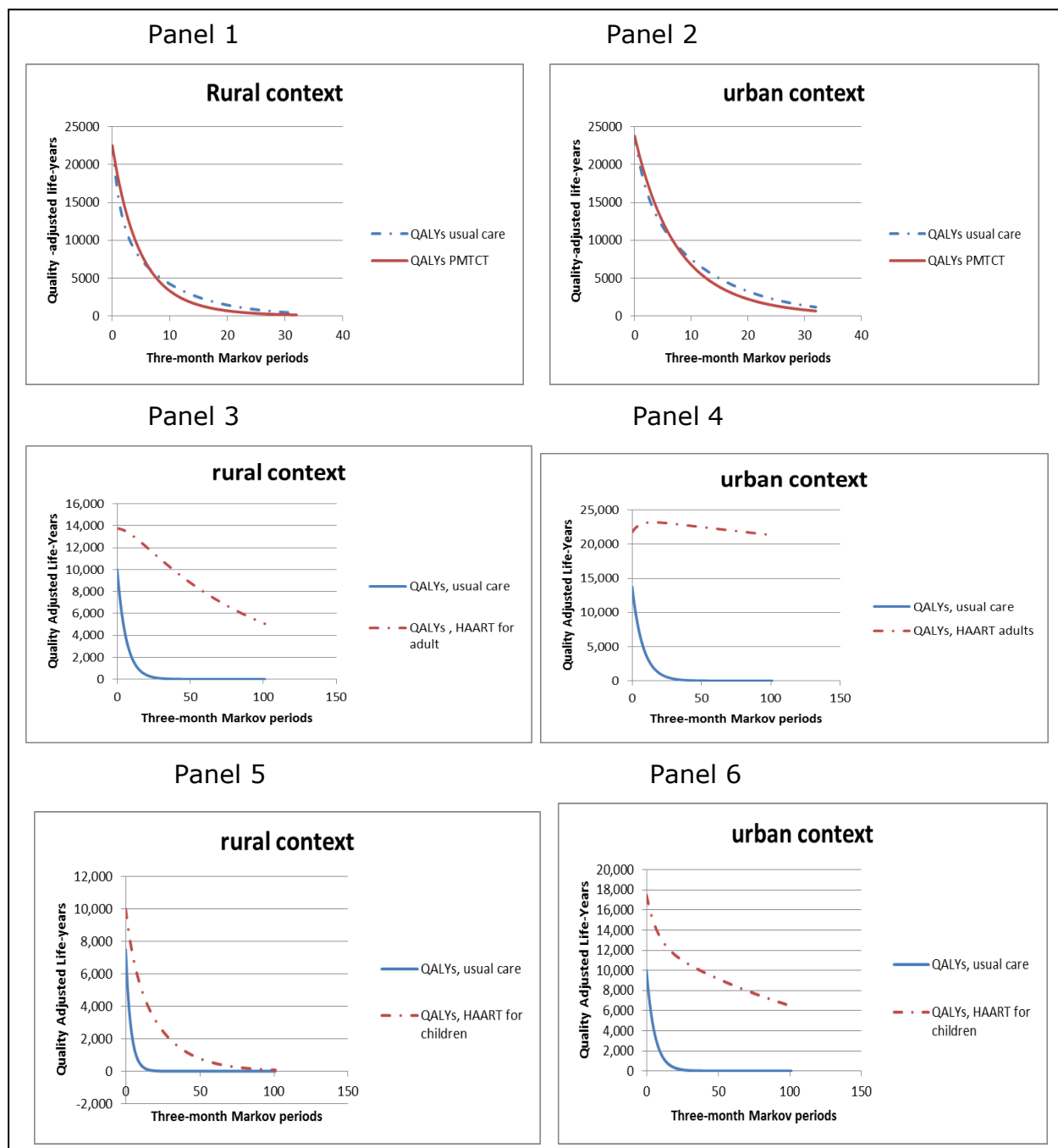
The cohort as well as the number of years in each 3-month period is constant. It follows that the patterns of effectiveness of HIV/AIDS interventions across contexts in terms of proportions surviving resemble the patterns of effectiveness of these interventions in terms of life-years gained. There is therefore no need to graphically represent this comparison and the conclusion drawn for survival as a measure of effectiveness applies to life-years gained.

8.2.2.4 Comparison of QALYs gained by an HIV/AIDS intervention across a rural context and an urban context

With quality adjusted life-years, the effectiveness pattern across a rural and an urban context might differ from that of survival measures because QALY measures involve quality of life which is different across rural and urban contexts²². Discounting also makes QALYs gained during later periods of

²² The quality of life data were obtained from quality of life studies in South Africa (Jelsma *et al.* 2006; O'Keefe *et al.*, 1996); Louwagie *et al.*, 2006). The quality of life in a rural context was approximated with the average

modelling worth less than QALYs gained in earlier periods. These considerations raise uncertainty about the comparability of the effectiveness of HIV/AIDS interventions in terms of QALYs across contexts. The results are illustrated in Figure 8:12.



Source: Author, based on the results of Markov models' simulations.

Figure 8:12 Comparison of effectiveness (QALYs) of HIV/AIDS interventions across a rural context and an urban context

quality of life of people who live predominantly a rural context, the black population. Similarly, the quality of life for the urban context was estimated on the basis of the average quality of life for the white population

As Figure 8:12 shows, except for PMTCT (Panel 1 and Panel 2), the results in terms of QALYs appear to be consistent with the results for survival (Panel 3 and Panel 4, Panel 5 and Panel 6). The results show that, in relation to USUAL CARE, HIV/AIDS interventions are generally more effective in the urban context than in the rural context when life-years adjusted for the quality of life (QALYs) are used as measures of effectiveness. As argued above, reweighting survival in the rural context with quality of life results in smaller quantities of QALYs.

8.2.3 Cost-effectiveness

A good grasp of the performance of an HIV/AIDS intervention in a rural and an urban context ultimately requires the joint consideration of cost and effectiveness. Cost-effectiveness estimates measured in terms of ICER are presented alongside numerical measures of incremental costs and incremental effectiveness. The statistics of interest to the analysis in this section are highlighted in Table 8:5.

Table 8:5 Lifetime cost (US\$), effectiveness (QALYs) and cost-effectiveness (US\$/QALY) for a cohort of 100,000 patients

Intervention	Rural context	Urban context	Value in a rural context as a % of the value in the urban context
USUAL CARE			
Total costs (GP)	146,700,000	319,400,000	46
Total costs (SP)	153,146,300	352,425,326	46
Total effectiveness (QALYs)	517,151	765,745	67
PMTCT			
Total costs (GP)	156,526,596	353,294,195	44
Total costs (SP)	162,589,125	361,152,326	43
Total effectiveness	580,142	884,672	65
Incremental costs	9,826,596	33,894,195	29
Incremental effectiveness (QALYs)	62,991	118,927	53
ICER (GP)	156	285	54
ICER (SP)	167	301	61
USUAL CARE			
Total costs (GP)	245,572,741	382,345,997	64
Total costs (SP)	251,156,256	390,126,326	63
Total effectiveness	1,955,943	2,178,923	89
HAART FOR ADULTS			
Total costs	858,139,181	952,828,151	89
Total effectiveness	2,088,378	3,186,842	65
Incremental costs	612,566,440	570,482,154	107
Incremental effectiveness (QALYs)	715,615	1,007,919	70
ICER (GP)	856	566	151
ICER (SP)	899	573	151
USUAL CARE			
Total costs	154,438,775	265,539,917	58
Total effectiveness	1,267,170	1,575,734	80
HAART FOR ADULTS			
Total costs GP	474,564,909	443,906,801	35
Total costs SP	482,546,312	450,123,156	36
Total effectiveness	2,109,841	2,547,809	82
Incremental costs	320,126,134	178,366,884	179
Incremental effectiveness (QALYs)	842,671	972,075	86
ICER (GP)	985	650	151
ICER (SP)	995	656	153

Source: Author, based on the results of Markov models' simulations.

As can be seen in Table 8.5, HIV/AIDS interventions and USUAL CARE, achieve more QALYs in an urban context than they do in a rural context. Furthermore, the incremental effectiveness of an HIV/AIDS intervention is generally greater in an urban context than in a rural context. For example, the incremental effectiveness of PMTCT in a rural context is 53% of its incremental effectiveness in the urban context. This may be explained by better living conditions in the urban context that promote effectiveness of PMTCT.

The table also shows that the total costs of an HIV/AIDS intervention and USUAL CARE are generally greater in an urban context than in a rural context. However, the incremental costs (IC) of each intervention over USUAL CARE do not follow this pattern. Table 8.5 shows that the IC of PMTCT in the rural context is less than the IC of PMTCT in the urban context. The IC of PMTCT in a rural context

represents 29% of its ICER in the urban context. However, the opposite is true for HAART FOR ADULTS and HAART FOR CHILDREN whose incremental costs in the rural context represent 107% and 179% of their respective IC in the urban context. This may be considered an obvious result since in the urban context one can expect greater usage and therefore greater cost of care.

Table 8:5 further shows that the ICER of PMTCT in a rural context is lower than its ICER in the urban context. Since ICER means cost per effectiveness, a lower ICER for PMTCT in a rural context means that PMTCT is more cost-effective in the rural context than it is in the urban context. The table shows that HAART FOR ADULTS and HAART FOR CHILDREN have greater ICERs in the rural context and consequently they are less cost-effective in this context. These results show that there is no specific pattern of CE common to all modelled interventions. In starting this study, this result was expected because of the expected complex interactions between the interventions, the factors in the contexts and the resulting outcomes.

The fact that HAART is less cost-effective in a rural context can be explained by a number of factors. First, HAART may be adding more to the costs of USUAL CARE than it adds to the effectiveness of USUAL CARE in the rural context, resulting in greater ICER in the rural context. Alternatively, HAART may be adding less to the costs of USUAL CARE than it adds to the effectiveness of USUAL CARE in an urban context.

If the equality of the CE of an HIV/AIDS intervention across contexts is defined as the equality of the ICERs of that intervention across these contexts, this implies that in case of such equality, the ICER value in Column 3 of Table 8:5 would be 100. The results in Table 8.5 show that the ICER value in column 3 varies to a greater extent around 100. Measuring the extent of the CE of an intervention across a rural and an urban context as the distance the ICER value is from 100, the extent of CE for modelled interventions becomes clear from Table 8.6.

Table 8:6 Summary comparison of cost-effectiveness of HIV/AIDS interventions in a rural context and an urban context (in US\$/outcome)

ICER rural	ICER urban	ICER in a rural context as % of ICER in an urban context
PMTCT		
156	285	54
HAART FOR ADULTS		
856	566	151
HAART FOR CHILDREN		
985	650	151

Source: Author, based on the results of Markov models' simulations.

Table 8:6 indeed shows that the extent of the CE of HIV/AIDS interventions is different. The table shows that HAART interventions are less cost-effective in the rural context than they are in the urban context. Their ICER relative to USUAL CARE in the rural context is greater than their ICER relative to USUAL CARE in the urban context. The ICERs in the rural context represent 151% of the ICERs in the urban context. In contrast, PMTCT is more cost-effective in rural contexts. Its ICER relative to USUAL CARE in the rural context is less than its ICER in the urban context to the extent that the ICER in the rural context represents 54% of the ICER in the urban context.

In summary, the results presented in Table 8:6 suggest that there is no specific trend in CE from a rural context to an urban context. Furthermore, the results show the different extent of CE across HIV/AIDS interventions. These results were subjected to probabilistic sensitivity analysis. Table 8:7 presents the results of this analysis.

Table 8:7 Results of probabilistic sensitivity analysis assuming no 2010 guidelines (US\$, 3% discount rate, government perspective)

Intervention	Average rural context		Average urban context	
	Cost (\$)	(QALYs)	Costs (\$)	QALYs
PMTCT USUAL CARE 95% CI	955 (833-3019)	8 (5-11)	2483 (1799-4593)	8 (6-13)
PMTCT 95% CI	1627 (187-1785)	12 (5-15)	3311 (1527-3504)	11 (6-16)
ICER	168		276	
HAART FOR ADULTS USUAL CARE 95% CI	2909 (2709-3114)	17 (6-33)	3822 (3627-4027)	6 (4-9)
HAART FOR ADULTS 95% CI	9909 (6821-13507)	19 (8-28)	17310 (6697-18497)	30 (17-42)
ICER	875		562	Percent=1353
HAART FOR CHILDREN USUAL CARE 95% CI	1543 (1355-1729)	4 (3-5)	2664 (2471-2853)	5 (4-6)
HAART FOR CHILDREN	5375 (3376-6756)	8 (5-11)	10,440 (4248-14633)	17 (9-25)
ICER	958		648	

Source: Author, based on the results of Markov models' simulations.

The results of the sensitivity analysis in Table 8.7 show that the conclusions of the base-case analysis do not change. They are, however, based on the evidence for the guidelines before 2010. Further sensitivity analysis is conducted to check the comparability of the interventions across contexts with the implementation of the 2010 guidelines. Following the guidelines for PMTCT and HAART issued in 2010, South Africa adopted earlier HAART treatment in 2011. Incorporating the available evidence on earlier treatment and earlier PMTCT in base-case values and conducting probabilistic sensitivity analysis, the results are reported in Table 8:8.

Table 8:8 Results of probabilistic sensitivity analysis with 2010 guidelines (3% discount rate, GP)

Intervention	Average rural context		Average urban context	
	Cost (\$)	(QALYs)	Costs (\$)	QALYs
PMTCT USUAL CARE 95% CI	1948 (833-3019)	8 (5-11)	3192 (1799-4593)	8 (6-13)
PMTCT 95% CI	2244 (255-2723)	10 (5-13)	3700 (1588-4497)	10 (7-14)
ICER	148		254	
USUAL CARE 95% CI	2909 (2709-3114)	17 (6-33)	3822 (3627-4027)	6 (4-9)
HAARTFOR ADULTS 95% CI	5264 (4325-10987)	20 (7-23)	15222 (6401-18350)	31 (18-43)
ICER	785		456	

Source: Author, based on the results of Markov models' simulations.

With earlier implementation of PMTCT and HAART, the cost per QALY gained decreases. However this does not affect the comparability of each intervention across the contexts.

8.3. Discussion of the results

The results in this chapter have shown that the ICER of all modelled HIV/AIDS interventions across a rural and an urban context are different. This is illustrated by the fact that the ICER of an HIV/AIDS intervention in a rural context as a percentage of the ICER in the urban context is not 100%. This result suggests that HIV/AIDS interventions are not equally cost-effective across a rural and an urban context as a result of many interrelated factors.

The results have also shown that the trends in CE across a rural and an urban context are not the same. The ICER of PMTCT is lower in the rural context than it is in the urban context, while the ICERs of HAART FOR ADULTS and HAART FOR CHILDREN are greater in the rural context than they are in the urban context. This result indicates an absence of consistent trends in the CE of HIV/AIDS interventions across a rural and an urban context. This observation can be explained by a number of factors. For example, stigma is more likely in rural contexts; this can decrease the intention to seek medical care. A trend would exist if the ICER of each HIV/AIDS intervention in a rural context as a

percentage of the ICER in the urban context is consistently lower or greater than 100%.

Further to the lack of consistent trends in the CE of HIV/AIDS interventions across a rural and an urban context, it is observed that the extent to which the ICER of an HIV/AIDS intervention in a rural context as a percentage of its ICER deviates from 100% is different across interventions. The ICER of PMTCT in a rural context as a percentage of its ICER in the urban context is 54%, while the corresponding percentages for HAART FOR ADULTS and HAART FOR CHILDREN are 125%. The fact that the ICERs in a rural context as a percentage of the ICERs in the urban are farther away from 100% for PMTCT than they are for HAART FOR ADULTS and HAART FOR CHILDREN shows that the extent of CE across modelled HIV/AIDS interventions is not the same.

With the ICER meaning the additional costs per health outcome, a lower ICER in a given context implies more cost-effectiveness. The evidence shows that PMTCT is more cost-effective in the rural context than it is in the urban context. By contrast, HAART FOR ADULTS and HAART FOR CHILDREN are less cost-effective in the rural context since their ICERs in this context represent 151% and 151%, respectively of their ICERs in the urban context.

An initial question was whether or not comparing the CE of HIV/AIDS interventions across a rural context and an urban context would result in different CE results. This question is answered by these results. Indeed, the results presented in this chapter have shown that the CE of HIV/AIDS intervention depends on contexts.

However, bearing in mind the design of CE in this chapter, the results are expected to be similar. In each context, the CE of an intervention was analysed on the same size cohort of patients, starting in the same HIV/AIDS state. The fact that the CE was shown to be different is at the centre of the rationale for this comparison.

One would have expected the cost of interventions to be lower in an urban context. Better standards of living in the urban context are expected to cushion

the degradation of health status as a result of HIV/AIDS, reduce the need to seek care and consequently reduced the costs of intervention over time. The higher costs in urban contexts may in this case be explained by higher levels of usage of health care in these contexts.

The comparison of HIV/AIDS interventions was grounded on the fact that the outcomes of HIV/AIDS interventions, particularly CE, are a result of the interaction between context, individual patients and the intervention. These factors, which have been theorised differently in the literature, are expected to prevail differently across a rural context and an urban context both in terms of trends and extent. In turn, these differences may influence the outcomes of interventions, especially when one acknowledges that HIV/AIDS interventions do not necessarily target all contextual and individual factors. Due to the fact that the analysis took these interactions into account by pegging the progression of patients in HIV/AIDS states over time, these results were expected, although there was no indication as to the trends and extent of CE across a rural context and an urban context or across HIV/AIDS interventions.

The observed extent of CE across HIV/AIDS interventions can be explained using the components of cost-effectiveness. The fact that PMTCT was more cost-effective in the rural context means that, relative to USUAL CARE, it achieves relatively more effectiveness given additional costs in the rural context compared with the urban context. Since PMTCT is conducted with pregnant women who use primary health care facilities in both rural and urban contexts, it is likely that the risk of infection is detected and prevented.

By contrast, with low HIV screening rates in rural contexts, the impact of the epidemic is detected too late when health status has already deteriorated. In the case of an urban context, better living conditions can cushion the impact, resulting in HAART interventions being relatively more effective in the urban context than in the rural context

Other studies have found that HIV/AIDS interventions have generally produced better effectiveness results in better socio-economic contexts (Kalitchman & Simbayi, 2006 for example). However, the rate of infections has been smaller in

lower socio-economic contexts in developing countries (Shisana and Simbayi, 2002). This supports the finding that, depending on the underlying factors, different outcomes of HIV/AIDS interventions can be observed in different contexts.

In a nutshell, one can conclude that the CE of HIV/AIDS interventions depends on the context. This conclusion has implications for South African policy makers. Policy makers, who have been allocating resources based on other considerations, could include consideration of the CE of HIV/AIDS interventions in socio-economic contexts to improve the efficiency of such interventions and so allocate their limited resources to the best effect.

The results of this study need to be considered with care in light of the cost and effectiveness evidence used. The cost and effectiveness data have limitations and the results may suffer in terms of accuracy. Despite these drawbacks, the study addressed the issue of uncertainty in order to ensure that its findings will be of value to policy makers in South Africa.

Chapter summary

In conclusion, this chapter compared the CE of HIV/AIDS interventions across a rural and an urban context using Markov models and QALYs as a measure of effectiveness. It compared the CE of an HIV/AIDS intervention in a rural context with the CE of that HIV/AIDS intervention in an urban context, taking into account the CE of USUAL CARE. The results show that generally, the effectiveness of HIV/AIDS interventions is lower in the rural context than in the urban context. The results also show that the costs in the rural context are lower than the costs in the urban context. In relation to the original research question of whether or not the CE of HIV/AIDS interventions depends on the context, the conclusion is that the CE of HIV/AIDS interventions indeed depends on the contexts. The policy implication is that policy makers should start considering the distribution of resources in HIV/AIDS interventions depending on contexts and on the extent of the CE of these interventions in such contexts. The next chapter analyses the CE of HIV/AIDS interventions in South Africa using projection models.

Chapter 9 : Cost-effectiveness of HIV/AIDS by epidemiological and socio-economic contexts

This chapter compares the CE of HIV/AIDS interventions across an LPC and a HPC and across a rural context and an urban context. Projection models are used to take account of the dynamics between HIV/AIDS interventions and contexts. The effectiveness for patients using HIV/AIDS interventions are projected over the period 2007-2020. Annual average costs are applied to projected patient-years using interventions. The effectiveness of an HIV/AIDS intervention is estimated in terms of infections and deaths averted by that intervention. Section one describes the methods, section two presents the results while section three discusses the results.

9.1 Methods

The incremental cost-effectiveness ratio (ICER) of an HIV/AIDS intervention relative to usual care (absence of an intervention) is calculated in each context and the ICERs of that HIV/AIDS intervention are compared across contexts. In epidemiological contexts, the ICER of an HIV/AIDS intervention in an LPC is compared to the ICER of that intervention in a HPC. In socio-economic contexts, the ICER of an HIV/AIDS intervention in a rural context is compared to the ICER of that intervention in an urban context.

The total costs and total health outcomes of an HIV/AIDS intervention and USUAL CARE in each of these contexts form the basis of the calculation of the ICER. The total costs of an HIV/AIDS intervention in a context is the sum of the annual costs over the period 2007-2020, obtained by multiplying the annual number of patients by the average annual cost. It is assumed that in the absence of an HIV/AIDS intervention, patients use USUAL CARE. Consequently, the total cost of USUAL CARE in a context is obtained by multiplying the annual average cost of USUAL CARE by the annual number of patients using an HIV/AIDS intervention and summing up the results over the period 2007-2020.

The annual number of patients in an LPC and a HPC from 2007 to 2020 are projected using the ASSA2008 AIDS model for each of the modelled HIV/AIDS

interventions. The projected numbers of patients for each HIV/AIDS intervention are also used for the intervention's USUAL CARE. The ASSA2008 AIDS model was explained in detail in Chapter 6.

The annual number of patients in a rural and an urban context over 2007-2020 is projected by the Spectrum Policy Modelling system (SPMS) for each of the modelled HIV/AIDS interventions. SPMS also projects the annual number of patients in a rural context and an urban context in the case of USUAL CARE (absence of an HIV/AIDS intervention). The SPMS was explained in detail in Chapter 6.

The evidence on the annual average costs of an HIV/AIDS intervention and USUAL CARE in a given context from the literature²³ is applied to annual numbers of patients to provide annual costs of interventions which are summed up over the period 2007-2020 to give the total cost of an intervention (or USUAL CARE). All costs are estimated in 2007 constant US\$ to control for inflation. The base-case comparison is conducted by taking into account the time preference with a discount rate of 3% as per the recommendation of an expert panel on cost-effectiveness analysis (Gold *et al.*, 1996), a coverage rate of 97%, and mean values of cost estimates.

Total health outcomes (total infections, deaths) of an intervention and total health outcomes of USUAL CARE in each context are obtained by summing up the projected annual health outcomes over the period 2007-2020. In epidemiological contexts (in an LPC and a HPC), annual health outcomes are produced by the ASSA2008 AIDS model projections while in socio-economic contexts (rural context and urban context) annual health outcomes are produced by SPMS projections.

The incremental cost of an HIV/AIDS intervention in each context is obtained by subtracting the discounted total cost, projected over 2007-2020, of USUAL CARE from the total costs, projected over 2007-2020, of an HIV/AIDS intervention.

²³ The state of knowledge at the moment allows the use of costs from the literature in the absence of cost data from the facilities. See for example Bachman (2006).

The incremental health outcomes (effectiveness) of an HIV/AIDS intervention in each context is obtained by subtracting the total health outcomes, projected over 2007-2020, of an HIV/AIDS intervention from the total health outcomes, projected over 2007-2020, of USUAL CARE. Since there are more infections and deaths in USUAL CARE than in an HIV/AIDS intervention, the effectiveness of the latter is expressed in terms of infections and deaths averted. The incremental costs and incremental effectiveness permitted the estimation of the ICER in each context for each intervention. The estimated ICERs were used to compare the CE of an intervention across contexts or to compare the CE across interventions.

The comparison of the CE of an HIV/AIDS intervention across epidemiological contexts and socio-economic contexts distinguishes the base-case comparison and scenario comparisons. The base-case comparison uses the evidence on the number of patients projected assuming a coverage rate of 97%, base-case values of annual cost estimates and a discount rate of 3%. In the first scenario, a decrease in the coverage rate is assumed. In the second scenario, the discount rate is changed to 0% and 7% following other literature in the country and the results are compared to the results of the base-case analysis. In the third scenario, upper and lower bound estimates of costs are used in the analysis and the results are compared to the results of the base- case analysis.

The analysis of these scenarios is based on the requirements of CE analysis to check how sensitive the results of the base-case analysis are to the most likely events. The analysis of the effect of a drop in the coverage rate of the intervention was due to potential reduction in the adherence to HIV/AIDS interventions. Long-lasting and widespread antiretroviral use resulted in an increase in risky behaviours in other parts of the world (McGowan *et al.*, 2004). With widespread antiretroviral therapy now available in South Africa, risky behaviours such as non-adherence to HIV/AIDS interventions, among others, are expected. The analysis of the effect of change in the discount rate is based on the recommendations by an expert panel on cost-effectiveness analysis (Gold *et al.*, 1996). The analysis of the effect of change in the cost-estimates is due to the fact that these costs are expected to be lower in the future, that they are very uncertain and that their evidence is insufficient.

9.2 Results in epidemiological contexts

This section presents the results in the epidemiological contexts. It presents the incremental cost, incremental effectiveness, and incremental cost-effectiveness.

9.2.2 Incremental costs

The incremental costs of HIV/AIDS interventions in a LPC and a HPC are presented in Table 9:1.

Table 9:1 Comparison of incremental costs of HIV/AIDS interventions in epidemiological contexts (2007-2020) in US\$

Low HIV prevalence areas				
Intervention	VCT	STD	PMTCT	HAART
Cost GP	389,328,120	598070904	658914257	2,117,371,410
Cost SP	475,845,480	755,497,409	733334410	2,758,929,249
USUAL CARE GP	0	271,447,392	352,720,802	743,725,574
USUAL CARE SP	0	318,126,185	418,126,185	802,024,941
IC GP	389,328,120	326.623,512	306193455	1,373,645,836
IC SP	475,845,480	437,371,224	315208225	1,956,904,308
Per 100,000 patients GP	409,500	5,600,000	8,208,000	10,940,000
Per 100,000 patients SP	495,000	5,721,890	5,412,125	11,295,000
High HIV prevalence areas				
Cost GP	735,386,670	1,686,275,335	1,466,349,264	5,594,011,845
Cost SP	742,128,040	1,874,097,366	1,525,891,975	5,932,044,036
USUAL CARE GP	0	1,110,433,585	749,204,264	2,153,993,925
USUAL CARE SP	0	1,289,139,491	799,823,225	2,301,299,316
IC GP	735,386,670	575,841,750	717,145,000	3,440,017,920
IC SP	742,128,040	584,957,875	726,068,750	3,630,744,720
Per 100,000 patients GP	327,600	5,381, 462	6, 566,400	6,968,153
Per 100,000 patients SP	380,012	5,482,563	6,782,186	7,122,146
IC/100,000 in an LPC over IC per 100,000 in HPC*100 GP	125%	104%	125%	157%

Source: Author, based on the results of ASSA model projections and annual estimates of costs. Keys: IC: incremental costs, GP: Costs evaluated from the perspective of the government, SP: Costs evaluated from the societal perspective.

Understandably, the extent of the cost of an HIV/AIDS intervention in each context is correlated with the number of patients in the intervention in that

context. This implies that an HIV/AIDS intervention will incur more incremental costs in a HPC than it does in an LPC because there are more patients in a HPC. Table 9.1 shows that the results are as per expectation. For example, using the government perspective costs, the incremental costs of VCT over the period 2007-2020 are US\$389,328,120 in an LPC while they are US\$585,702,432 in a HPC. Therefore, a plausible comparison of incremental costs of an HIV/AIDS intervention across an LPC and a HPC requires the control of the number of patients. Controlling for the size of the population of patients by comparing the incremental cost per 100,000 patients across contexts, the results show that the incremental costs are lower in a HPC. Per 100,000 patients, these costs are US\$327,600 in a HPC while they are US\$409,500 in an LPC, using government perspective costs. The lower costs in an HPC are shown by the results in the last row of Table 9:1, which displays the incremental costs in an LPC as a percentage of the incremental costs in a HPC. The percentage is greater than 100%, indicating that incremental costs in an LPC per 100,000 patient-years are greater than corresponding costs in a HPC. These results appear to concur with the evidence in the literature that the scale of the intervention results in lower costs (Dandona *et al.*, 2008).

9.2.1 Incremental effectiveness

As discussed in the analysis of costs, it is not plausible to compare incremental effectiveness across an LPC and a HPC without controlling for the size of the population of patients because these contexts have a different number of patients. To control for the difference in the number of patients, the incremental effectiveness is analysed per 100,000 patient-years in each context. The incremental effectiveness results of each HIV/AIDS intervention modelled in an LPC and a HPC are presented in Table 9:2.

Table 9:2 Comparison of incremental effectiveness (IE) of HIV/AIDS interventions in epidemiological contexts (2007-2020)

Low HIV prevalence contexts				
Intervention	VCT	STD	PMTCT	HAART
Absence Total infection Total deaths	264, 617 -	271,032 -	309,933 -	723,743
Presence Total infection Total deaths	254,761	248,188	248,188	366,120
IE (infections and deaths averted)	9,856	22,844	61,745	357,623
IE (infections and deaths averted per 100,000 patient-years)	189 Infections	18,900 Infections	56,600 Infections	75,500 Deaths
High HIV prevalence contexts				
Intervention	VCT	STD	PMTCT	HAART
Presence Total infection Total deaths	1 141,559	1,114,080	1,113,870	4,244,879
Absence Total infection Total deaths	1,153,205	1,153,205	1,194,995	4,678,349
IE (infections and deaths averted)	11,646	39,125	81,125	433,470
IE (infections and deaths averted per 100,000 patient-years)	156 Infections	16,200 Infections	65,800 Infections	41,900 Deaths
Infection averted per 100,000 patients in an LPC over infection averted per 100,000 patients *100	121%	116%	102%	115%

Source: Author, based on the projections of ASSA2008 AIDS model. Note: the percentage under the IE figure in an LPC denotes that estimate as a percentage of the effectiveness of the same intervention in a HPC.

This Table shows that the incremental effectiveness of each HIV/AIDS intervention in an LPC is greater than its incremental effectiveness in a HPC. For instance, the incremental effectiveness of VCT in terms of infections averted per 100,000 patients is 189 in an LPC while the corresponding statistic in a HPC is 156. In terms of relative comparison, the incremental effectiveness of VCT in an LPC is 121% of its incremental effectiveness in a HPC and this pattern of results applies to other modelled interventions. Since the incremental effectiveness is higher in an LPC for all modelled interventions, the latter are more effective in an LPC.

9.2.3 Cost-effectiveness

This section compares joint cost and effectiveness across contexts for modelled interventions. These results are in Table 9:3.

Table 9:3 Comparison of ICERs of HIV/AIDS interventions in epidemiological contexts (2007-2020)

Low HIV prevalence areas				
Intervention	VCT	STD	PMTCT	HAART
cost GP	389,328,120	598070904	658914257	2,117,371,410
cost SP	475,845,480	755,497,409	733334410	2,758,929,249
USUAL CARE GP	0	271,447,392	352,720,802	743,725,574
USUAL CARE SP	0	318,126,185	418,126,185	802,024,941
IC GP	389,328,120	326,623,512	306193455	1,373,645,836
IC SP	475,845,480	437,371,224	315208225	1,956,904,308
Incremental effectiveness	9,856	22,844	61,745	257,623
ICER GP	39,496	14,298	4,959	5,332
ICERSP	48,279	19,858	5,105	7,596
High HIV prevalence areas				
cost GP	735,386,670	1,686,275,335	1,466,349,264	5,594,011,845
cost SP	742,128,040	1,874,097,366	1,525,891,975	5,932,044,036
USUAL CARE GP	0	1,110,433,585	749,204,264	2,153,993,925
USUAL CARE SP	0	1,289,139,491	799,823,225	2,301,299,316
IC GP	735,386,670	575,841,750	717,145,000	3,440,017,920
IC SP	742,128,040	584,957,875	726,068,750	3,630,744,720
Incremental effectiveness	11,646	39,125	81,125	433,470
ICER GP	63,145	14,718	8,840	7,936
ICER SP	63,723	14,951	8,950	8,375
ICER LPC/ICERHPC*100	62%	97%	56%	67%

Source: Author, based on the results of ASSA2008 AIDS model projections. The percentage is the value of ICER in an LPC as a percentage of ICER in a HPC.

Table 9:3 shows that the ICERs of all modelled HIV/AIDS interventions relative to their respective USUAL CARE are lower in an LPC than they are in a HPC. For instance, the ICER of VCT is US\$39,496 for each infection averted in an LPC while its ICER in a HPC is US\$63,145. This pattern of ICER across an LPC and a HPC is also true for STD, PMTCT and HAART. This result shows that generally, modelled HIV/AIDS interventions are more cost-effective in an LPC than they are in a HPC.

It should be noted, however, that, although the CE effectiveness of HIV/AIDS interventions is generally greater in an LPC than it is in a HPC, the extent of CE is different across HIV/AIDS interventions. Table 9:4 shows the results.

Table 9:4 Comparison of the extent of cost-effectiveness across HIV/AIDS interventions in epidemiological contexts (in US\$/outcome)

ICER LPC	ICER HPC	ICER in an LPC as % of ICER in a HPC
VCT		
39,496	63,145	62
STD		
14,298	14,718	97
PMTCT		
4,959	8,840	56
HAART		
5,332	7,936	67

Source: Author, based on the results of ASSA2008 AIDS model projections.

To understand the comparison of the extent of CE across modelled HIV/AIDS interventions in Table 9:4, it is worth starting with a situation in which the extent of the CE of an HIV/AIDS intervention is the same across contexts. An HIV/AIDS intervention is equally cost effective in an LPC and a HPC if Column 3 of Table 9:4 is 100%, that is, the ICER of an HIV/AIDS intervention in an LPC is equal to the ICER of that HIV/AIDS intervention in a HPC. The farther the value in Column 3 is from 100%, the more the CE of an HIV/AIDS intervention in an LPC is unequal to the CE in a HPC. In particular, if an intervention has a lower ICER in an LPC than it has in a HPC, it is more cost-effective in an LPC. Since the values in column 3 of Table 9:4 are less than 100%, each of the modelled HIV/AIDS interventions is more cost-effective in an LPC. However the extent of CE measured by how far the value is from 100%, suggests a different extent of CE across HIV/AIDS interventions. PMTCT for instance, emerges as the most cost-effective because the value in Column 3 for PMTCT is farthest from 100% and STD is the least cost-effective in an LPC because the value in Column 3 for STD is closest to 100%.

These results are subjected to scenario analysis. In this analysis, the conclusion reached in the base-case analysis with 97% coverage rate is assessed against the assumption of a decrease in the coverage rate by 20%. Table 9:5 shows the results.

Table 9:5 Effect of a decrease in coverage rate by 20%, government perspective.

Decrease by 20% in an LPC, other parameters remaining unchanged				
VCT				
ICER LPC		ICER HPC		ICER in a HPC as % of ICER in an LPC
Base-case	39,496	Base-case	83,820	47
Decrease	41,125	Base-case	83,820	49
STD				
Base-case	14,298	Base-case	14,718	97
Decrease	14,595	Base-case	14,718	99
PMTCT				
Base-case	13,052	Base-case	14,498	90
Decrease	13,512	Base-case	14,498	68
HAART				
Base-case	5332		7936	67
Decrease	5,515		7,936	66
Decrease by 20% in a HPC, other parameters remaining unchanged				
ICER LPC		ICER HPC		
VCT				
Base-case	39,496	Decrease	83,820	47
Base-case	39,496	Base-case	83,650	49
STD				
Base-case	14,298	Decrease	14,718	97
Base-case	14,298	Base-case	15,250	87
PMTCT				
Base-case	13,052	Decrease	14,495	90
Base-case	13,052	Base-case	14,952	88
HAART				
Base-case	5,332	Decrease	7936	67
Base-case	5,332	Base-case	8300	67

Source: Author, based on the results ASSA2008 AIDS model projections and annual estimates of costs

Table 9:5 shows that a decrease in the coverage of HIV/AIDS interventions by 20% in an LPC increases their ICERs in this context. The Table also shows that a decrease in the coverage of HIV/AIDS interventions by 20% in a HPC increases their ICERs in that context. For example, the ICER of VCT in an LPC changes from US\$39,496 in the base-case comparison to US\$41,125 in the case of a decrease in the coverage of VCT by 20%. The Table shows further that the effect of a decrease in the coverage observed for VCT is true for other modelled interventions. Indeed an assumption of decrease in the coverage by 20% in an LPC or a HPC makes the ICER of all interventions increase. An implication of this result is that the effectiveness of the modelled HIV/AIDS interventions decreases more than the decrease in the cost as a result of reduction in the coverage by 20%. It is however, worth noting that, despite the change in the ICER as a result of the reduction in the coverage of HIV/AIDS interventions, this change in ICER does not significantly affect the comparability of the CE of HIV/AIDS interventions across an LPC and a HPC. Column 3 of the Table shows that the

ICER of each intervention in an LPC is less than 100% of the ICER in a HPC, indicating no change in the patterns of cost-effectiveness of HIV/AIDS interventions from the patterns observed in the base-case comparison.

The conclusion of the base-case comparison was also assessed against the change in the discount rate. Table 9.6 shows the CE results under different discount rates.

Table 9:6 Effect of using different discount rates, government perspective.

VCT			
	LPC	HPC	ICER in a HPC as % of ICER in an LPC
Discount rate	ICER	ICER	
(0%)	45,125	93,125	48
(3%)	39,496	83,820	47
(7%)	33,135	63,125	41
STD			
(0%)	17,250	18,251	96
(3%)	14,298	14,718	97
(7%)	9,156	10,250	96
PMTCT			
(0%)	5,298	9,294	57
(3%)	4,959	8,840	56
(7%)	3,785	5,758	56
HAART			
(0%)	6,768	9,808	69
(3%)	5,332	7,936	67
(7%)	4,218	6,390	66

Source: Author, based on the results of ASSA2008 AIDS model projections models.

The Table shows, as expected, that the ICERs of modelled HIV/AIDS interventions decrease as the discount rates increase. The results show for example that with a discount rate of 3%, the ICER of VCT relative to USUAL CARE of US\$ 39,496 in an LPC changes to 33,135 with a discount rate of 7%. The same patterns in the change of ICER are observed in a HPC as the discount rate increases from the base-case discount rate of 3% to a discount rate of 7%. While these changes are observed for all modelled HIV/AIDS interventions, they do not change the base-case conclusion that all modelled HIV/AIDS interventions are more cost-effective in an LPC than they are in a HPC.

In contrast, using lower and upper bound cost-estimates reveals that the changes in the cost estimates affect the conclusions reached by the base-case comparison. Table 9.7 shows these results.

Table 9:7 Effect of using lower and upper bound cost estimates

ICER LPC	ICER HPC	ICER HPC as % of ICER of an LPC
VCT		
39,496 (mean cost)	83,820	47
34,315 (lower cost)	33,453	105
105,000 (upper limit)	99,000	115
STD		
14,298 (mean cost)	14,718	97
7,156 (lower limit)	6,156	125
16,215 (upper limit)	16,700	99
PMTCT		
13,052 (mean cost)	14,498	90
11,125 (lower limit)	12,156	91
16,156 (upper limit)	17,189	92
HAART		
7704 (mean cost)	4274	151
5235 (lower limit)	3250	549
9250 (upper limit)	7630	159

Source: Author, based on the results of epidemiological projection models, scenario analysis.
The conclusions apply to the results when costs are evaluated from the societal perspective.

As Table 9.7 shows, some interventions which are more cost-effective in an LPC become less cost-effective as a result of a change in the cost estimates. For instance VCT and STD, which are more cost-effective in an LPC when the base-case estimates of costs are used, become less cost-effective in that context when the lower bound estimates of costs are used. The results show, for example that VCT is more cost-effective in an LPC than it is in a HPC, with ICERs in these contexts being US\$39,496 and US\$ 83,820, respectively. This result arises when the median costs of the base-case comparison are used. When the lower bound cost estimates are used however, VCT becomes less cost effective in an LPC than it is in a HPC. The data in Table 9.7 show that in the case of lower bound cost-estimates, the ICER of VCT relative to USUAL CARE in an LPC is US\$34,315 while the similar statistic in a HPC is US\$33,453. The discussion about the change in the CE of VCT across an LPC and a HPC as a result of a change in cost estimates applies to STD. In sum, a change in the cost affects the conclusion of the base-case comparison.

9.3 Results in socio-economic contexts

This section presents the results in socio-economic contexts. The costs, the effectiveness, and CE results are presented.

9.3.1 Costs

The cost results are presented in Table 9:8. These costs are obtained by applying the average annual cost per patient to the number of patient-years using interventions over the period of analysis, as projected by SPMS.

Table 9:8 Comparison of incremental costs of HIV/AIDS interventions in socio-economic contexts (2007-2020)

Rural context			
Intervention	PMTCT	HAART FOR ADULTS	HAART FOR CHILDREN
Total cost USUAL CARE GP	459,054,600	892,784,873	105,911,427
Total cost USUAL CARE SP	463,149,140	982,063,361	116,502,569
Total cost of intervention GP	618,810,422	1,205,259,579	185,344,996
Total cost of intervention SP	692,676,440	1,249,898,823	195,936,139
ICER GP per 100,000 patients	159,755,822	1,300,420,072	245,913,118
ICER SP per 100,000 patients	229,527,300	267,835,462	79,433,570
Urban context			
Total cost USUAL CARE GP	437,165,992	3,190,138,899	212,427,251
Total cost USUAL CARE SP	453,748,675	3,312,836,549	155,043,316
Total cost of intervention GP	675,607,516	3,987,673,624	298,971,687
Total cost of intervention SP	575,553,200	4,294,417,749	314,707,039
IC GP per 100,000 patients	238,441,525	2,483,740,496	379,740,496
IC SP per 100,000 patients	251,804,525	592,202,559	102,279,788
IC per 100,000 patients GP rural /IC per 100,000 patients GP *100	67%	143%	103%

Source: Author, based on the results of SPMS projections. Key: GP: government perspective; SP: societal perspective. The percentage reflects the value of the incremental costs of an HIV/AIDS intervention in a rural context as a percentage of the incremental costs of that intervention in an urban context for 100,000 patient-years.

As the Table shows, the incremental cost per 100,000 patients is generally higher in a rural context than it is in an urban context for HAART FOR ADULTS and HAART FOR CHILDREN. For PMTCT however, the incremental cost is lower in the rural context than it is in an urban context. Table 9:8 shows, for example, that, using government perspective costs, PMTCT results in an incremental cost of US\$159,755,822 in a rural context while the incremental costs in an urban context are US\$238, 441,525. The higher incremental cost of HAART

interventions in a rural context can be attributed to reduced economies of scale although other factors such as seeking treatment too late may also play a role.

9.3.2 Effectiveness

After comparing the costs across a rural and an urban context, it is useful to compare the effectiveness of HIV/AIDS interventions across these contexts. The effectiveness measures used in this comparison are infections and deaths averted by an HIV/AIDS intervention relative to USUAL CARE. Table 9:9 shows the results.

Table 9:9 Comparison of incremental effectiveness of HIV/AIDS interventions in socio-economic contexts (2007-2020)

Intervention	Effectiveness	
	Rural context	Urban context
No intervention at all		
Cumulative paediatric infections	315,258	505,661
Cumulative adult deaths	2,119,490	3,528,417
Cumulative paediatric deaths	222,628	353,781
PMTCT		
Total infections with PMTCT	198,392	314,987
Paediatric infections averted by PMTCT	116,866	193,164
HAART FOR ADULTS		
Total adult deaths with HAART FOR ADULTS	1,590,003	2,077,634
Total adult deaths averted by HAART FOR ADULTS	529,487	1,450,783
HAART FOR CHILDREN		
Total child deaths with HAART FOR CHILDREN	108,523	170,376
Total child deaths averted by HAART FOR CHILDREN	114,105	183,405

Source: Author, based on the results of SPMS projections.

Table 9:9 shows that for each HIV/AIDS intervention, the number of infections (deaths) averted by an HIV/AIDS intervention relative to USUAL CARE is greater in an urban context than it in a rural context. For instance, PMTCT averts 198,398 infections over the period 2007-2020 in a rural context while it averts 314,986 infections in the urban context over the same period. However, this finding needs to be considered in relation to the size of the population in these

contexts. The fact that there are more patients in an HIV/AIDS intervention in an urban context might lead to greater effectiveness in this context.

The effectiveness of an HIV/AIDS intervention across a rural and an urban context is better grasped if the difference in the number of patients across these contexts is controlled for. To control for the number of patients, estimates of effectiveness are reported per 100,000 patients in each context. Table 9:10 shows the results.

Table 9:10 Comparison of incremental effectiveness of HIV/AIDS Interventions in socio-economic contexts per 100,000 patient-years (2007-2020)

HIV outcomes	Rural context		
	PMTCT	HAARTA	HAARTC
A1. Total patient-years	893,972		
B1. Total infections averted	116,866		
C1. Averted infections per 100,000 patient-years	77,400		
A1. Total patient-years		5,693,664	
B1. Total adult deaths averted by HAARTA		529,487	
C1. Averted infections per 100,000 patient-years		68,700	
A1. Total patient-years			663,813
B1. Total child deaths averted by HAARTC			108,523
C1. Averted infections per 100,000 children-years			58,500
HIV outcomes	Urban context		
	PMTCT	HAARTA	HAARTC
A2. Total patient-years	1,472,686		
B2. Total infections averted	190,674		
C2. Averted infections per 100,000 patient-years	88,700		
A2. Total patient-years		15,649,025	
B2. Total adult deaths averted by HAARTA		1,450,783	
C2. Averted infections per 100,000 patient-years		71,600	
A2. Total patient-years			987,837
B2. Total child deaths averted by HAARTC			183,405
C2. Averted infections per 100,000 children-years			61,500
C1/C2*100	91%	65%	80%

Source: Author, based on SPMS projections. Key: HAARTA: HAART FOR ADULTS, HAARTC: HAART FOR CHILDREN.

As Table 9:10 indicates, modelled HIV/AIDS interventions are less effective in a rural context than they are in an urban context. The Table shows that per 100,000 patient-years, PMTCT prevent less HIV infections in the rural context than it does in the urban context. In fact, the intervention prevents 77,400

infections in a rural context while it prevents 88,700 infections in the urban context.

Similarly, HAART FOR ADULTS and HAART FOR CHILDREN prevent fewer deaths in the rural context. Per 100,000 patient-years, HAART for ADULTS prevents 68,700 HIV/AIDS deaths in the rural context while it prevents about 71,600 HIV/AIDS deaths in the urban context. Corresponding statistics of HIV/AIDS deaths averted by HAART FOR CHILDREN in a rural context and an urban context are 58,500 and 61,500. Because less HIV infections and HIV/AIDS deaths are averted in the rural context, the incremental effectiveness in a rural context expressed as percentage of the incremental effectiveness in an urban context is less than 100%. The last row of Table 9.10 shows that this percentage ranges from 65% to 91% for all modelled HIV/AIDS interventions.

9.3.3 Cost-effectiveness

In CE analysis, it is important to analyse the additional costs that induce additional benefits. To take account of the full effect of contexts on the cost and effectiveness of HIV/AIDS interventions, the ICER of an HIV/AIDS intervention relative to USUAL CARE is reported and the ICERs of the same intervention are compared across contexts, in the base-case comparison. Table 9:11 shows the results.

Table 9:11 Comparisons of ICERs of HIV/AIDS interventions in socio-economic contexts (2007-2020)

Rural context			
Description	PMTCT	HAARTA	HAARTC
Total cost USUAL CARE GP	162,570,017	892,784,873	105,911,427
Total cost USUAL CARE SP	177,349,110	982,063,361	116,502,569
Total cost of intervention GP	221,686,387	1,205,259,579	185,344,996
Total cost of intervention SP	243,855,026	1,249,898,823	195,936,139
Incremental cost of intervention GP	159,755,822	1,300,420,072	245,913,118
Incremental cost of intervention SP	66,505,916	267,835,462	79,433,570
ICER GP	1,367	2,456	2,266
ICER SP	1,456	2,512	2,302
Urban context			
Total cost USUAL CARE GP	73,895,462	3,190,138,899	212,427,251
Total cost USUAL CARE SP	88,674,555	3,312,836,549	155,043,316
Total cost of intervention GP	466,705,815	3,987,673,624	298,971,687
Total cost of intervention SP	484,889,158	4,294,417,749	314,707,039
Incremental cost of intervention GP	387,830,916	2,483,740,496	379,740,496
Incremental cost of intervention SP	396,214,603	592,202,559	102,279,788
ICER GP	2,034	1,712	2,070
ICER SP	2,185	1,912	2,149
ICER rural GP/ICER urban GP *100	67%	143%	109%

Source: Author, based on the results of SPMS projections. Key: GP: government perspective, SP: societal perspective. HAARTA: HAART FOR ADULTS, HAARTC: HAART FOR CHILDREN. The percentage in the last row of Table 9.11 reflects the value of the ICER in a rural context as a percentage of the ICER in an urban context for a given HIV/AIDS intervention.

The results in Table 9:11 indicate that PMTCT is relatively more cost-effective in a rural context than it is in an urban context. The ICER for PMTCT in the rural context is US\$1,367 per infection averted in the rural context while its ICER in the urban context is US\$2,034 per infection averted. In terms of relative cost-effectiveness, the ICER of PMTCT in the rural context is 67% of its ICER in the urban context. Therefore, PMTCT is relatively more cost-effective in the rural context. As noted earlier, this could be the result of complex factors, mainly pertaining to costs in the rural areas, where lower costs are due to the fact that PMTCT is linked to antenatal care provided by rural clinics.

HAART FOR ADULTS and HAART FOR CHILDREN are more cost-effective in the urban context than they are in a rural context. Their ICERs are US\$2,456 and US\$2,266, respectively per death averted in the rural context while these ICERs are US\$1,712 and US\$2,070 per death averted in the urban context. In terms of relative cost-effectiveness, the ICERs of HAART FOR ADULTS and HAART FOR CHILDREN in the rural context are 143% and 109% of their respective ICERs in the urban context. These results show that HAART FOR ADULTS and HAART FOR CHILDREN are relatively less cost-effective in the rural context. This result is

expected since the effectiveness of these interventions is expected to be lower in the rural context and the costs are expected to be lower in the urban context because of timely use of care.

Furthermore, the results in Table 9:11 show that, the extent of CE varies across HIV/AIDS interventions. The extent of effectiveness in any context is measured by how close the ICER of an HIV/AIDS intervention in one context expressed as a percentage of the ICER of that intervention in another context is to 100%. Table 9:11 shows that the ICER of HAART FOR ADULTS in the rural context as a percentage of the ICER of HAART in the urban context is the farthest from 100%. This implies that HAART has the greatest extent of cost-effectiveness in the urban context. The different extent to which the ICERs of modelled HIV/AIDS interventions are close to 100% in Column 3 of Table 9.12 indicates the different extent of cost-effectiveness across the modelled HIV/AIDS interventions.

Table 9:12 Comparison of the extent of cost-effectiveness across HIV/AIDS interventions in socio-economic contexts (in US\$/outcome)

ICER rural	ICER urban	ICER in a rural context as % of the ICER in an urban context
PMTCT		
1367	2034	54
HAART FOR ADULTS		
2456	1712	151
HAART FOR CHILDREN		
2266	2070	109

Source: Author, based on the results of SPMS projections

Briefly, the results in Table 9.12 illustrate that the CE of HIV/AIDS interventions has no specific trend across a rural context and an urban context as some HIV/AIDS interventions are more cost-effective in the rural areas, while for others the opposite is true. The results also show that the extent of CE is different across interventions.

These results are subjected to sensitivity analysis. One of the key issues likely to affect the effectiveness of HIV/AIDS interventions requiring lifelong therapy, HAART, is a decrease in treatment adherence. As this would affect the coverage of HIV/AIDS interventions, the chapter analyses the effect of a 20% decrease in

coverage (due to a possible decrease in adherence) on the results of the base-case comparison. The results are presented in Table 9:13.

Table 9:13 Effect of a decrease in coverage rate by 20%, government's perspective.

Adherence drop by 20% in rural context				
Rural context				
		PMTCT	HAART A	HAART C
Base-case	ICER GP	1367	576	2,281
Drop 20%	ICER GP	1417	494	2,632
Urban context				
Base-case	ICER GP	2034	550	2,067
Drop 20%	ICER GP	2034	550	2,067
Adherence drop by 20% in urban context				
Rural context				
		PMTCT	HAART A	HAART C
Base-case	ICER GP	1367	2452	2,266
Drop 20%	ICER SP	1367	2452	2,266
Urban context				
Base-case		1,914	540	2,044
Drop 20%		1,923	665	2,215

Source: Author, based on the results of SPMS projections. GP: government perspective costs, SP: societal perspective costs, HAART A: HAART FOR ADULTS, HAART C: HAART FOR CHILDREN.

It is observed that a 20% decrease in adherence in one context does not affect the result of the base-case estimates in another context but only the estimates in the context in which the decrease takes place. For instance, a 20% decrease in adherence in the rural context does not affect the ICER of PMTCT in the urban context. The ICER of PMTCT remains equal to the ICER of the base-case comparison, that is, US\$2,034. When there is 20% decrease in adherence in the rural context, the ICER of HIV/AIDS interventions in the rural context increases. For instance, the ICER of PMTCT increases from US\$1,367 to US\$1,417. This result implies that the effectiveness of modelled HIV/AIDS interventions decreases more than the decrease in the cost as a result of a 20% reduction in coverage.

Similarly, a 20% decrease in adherence in the urban context does not affect the results of the base-case comparison in the rural context. However, this decrease in adherence increases the ICER of HIV/AIDS interventions in an urban context. Table 9.13 shows that the ICER of PMTCT in an urban context, for instance, increases from US\$1,914 to US\$1,923. Again, this signifies that, as a result of 20% decrease in adherence in a given context, the decrease in effectiveness is

more than the decrease in costs. However, even though a decrease in adherence affects the CE of an intervention in the context in which the decrease takes place, it does not affect the comparability of the CE of HIV/AIDS interventions across contexts. Therefore the results of the base-case comparison are robust to the change in adherence.

The discount rates used have been considered as factors influencing the CE results. Consequently, it was recommended (Gold *et al.*, 1996) that studies examine how the conclusions of the base-case comparison change with different discount rates. To this end, the CE results of the base-case comparison were reproduced using different discount rates. Table 9:14 shows the ICER of HIV interventions under alternative discount rates.

Table 9:14 Effect of using different discount rates

Discount rate		Rural area			Urban areas		
		PMTCT	HAART	HAARTC	PMTCT	HAART	HAARTC
0%	ICER GP	1654	645	2,830	2,472	701	2,595
	ICER SP	1805	753	3,266	2,494	863	2,812
3%	ICER GP	1367	590	2,266	2034	550	2,067
	ICER SP	1492	606	2,605	2051	667	2,239
7%	ICER GP	1089	438	1,714	1,609	408	1,567
	ICER SP	1188	984	1,815	1,623	502	1,697

Source: Author, based on the results of SPMS projections. ICER is measured as costs per infection averted for PMTCT, per death averted for HAART interventions. Key: GP: government perspective costs, SP: societal perspective costs.

As expected, the Table shows that the ICERs of HIV/AIDS interventions decrease as the discount rates increases. The results show for example, that with a discount rate of 3%, the ICER of PMTCT of US\$1,367 (measured from the government perspective) in a rural context changes to US\$1,089 with a discount rate of 7%. The same patterns in the change of ICER are observed in an urban context. While these changes are observed for all modelled interventions, they do not change the base-case conclusion that all modelled HIV/AIDS interventions are more cost-effective in an LPC than they are in a HPC.

Finally, the insufficiency of cost data evidence required a scenario analysis of what would happen to the base-case conclusions when the lower and upper bound estimates of costs were used. Table 9:15 shows the results.

Table 9:15 Effect of using lower and upper bound cost estimates

Lower bound estimates			
Rural context			
ICER/ Intervention	PMTCT	HAART	HAARTC
ICER GP	685	632	735
ICER SP	752	759	750
Urban context			
ICER/Intervention	PMTCT	HAART	HAARTC
ICER GP	1,050	803	656
ICER SP	1,115	830	690
Upper bound estimates			
Rural context			
ICER/Intervention	PMTCT	HAART	HAARTC
ICER GP	2300	1265	2150
ICER SP	2548	1560	2250
Urban context			
ICER/Intervention	PMTCT	HAART	HAARTC
ICER GP	1,850	1315	2400
ICER SP	2,836	1395	2420

Source: Author, based on the results of SPMS projections. Key: GP: government perspective costs, SP: societal perspective costs.

The results in Table 9:15 show that the use of lower and upper bound cost estimates changes some of the conclusions in the base-case analysis. For instance, in the base-case comparison, PMTCT was more cost-effective in the rural context. While the intervention remains more cost-effective with the use of lower-bound cost estimates, the opposite is true when upper bound cost-estimates are used. Table 9:15 shows that with upper bound estimates of costs, the ICER of PMTCT in a rural context becomes US\$2,300 per infection averted while it is US\$1,850 per infection averted in an urban context. This result makes PMTCT more cost-effective in the urban context; this conclusion is different from the conclusion in the base-case comparison. The change in the cost-effectiveness comparability of PMTCT across a rural context and an urban context as a result of a change in cost estimates applies to other modelled interventions. HAART FOR ADULTS, which was more cost-effective in the urban context, becomes less cost-effective when lower bound cost estimates are used

as shown in Table 9:15. As the results in Table 9:15 change many of the conclusions reached by the base-case comparison, the results are not robust to change in estimates of cost.

9.4 Discussion of the results

One of the research questions in this thesis was whether or not the CE of an HIV/AIDS intervention depends on contexts. In epidemiological contexts, the results presented above show that the ICER of each intervention in an LPC as a percentage of its ICER in a HPC is less than 100%.

While the ICER of each HIV/AIDS intervention in an LPC is consistently lower than the ICER of that intervention in a HPC, this is not the case in socio-economic contexts. The ICER of PMTCT in the rural context as a percentage of its ICER in the urban context is 67%. In contrast, the ICERs of HAART FOR ADULTS and HAART FOR CHILDREN in rural contexts are 151% and 109%, respectively of the ICERs in the urban context.

Bearing in mind that the ICER of an intervention is the additional costs per additional health outcomes of an intervention as compared to USUAL CARE, the lower the ICER, the more cost-effective the intervention. Linking this information to the results above, it is clear that an HIV/AIDS intervention is not equally cost-effective across epidemiological contexts and across socio-economic contexts. If an intervention was equally cost-effective across contexts, its ICER in one context as a percentage of its ICER in another context would be 100%.

Although there is a difference in the CE of an intervention from one context to another, the CE trends depend on whether the contexts are epidemiological or socio-economic. In epidemiological contexts, the CE of each HIV/AIDS intervention is consistently higher in an LPC than in a HPC, while in socio-economic contexts, how the CE of an HIV/AIDS intervention in a rural context compares with its CE in an urban context depends on the intervention. For instance, PMTCT is more cost-effective in rural contexts while HAART for ADULTS and HAART FOR CHILDREN are less cost-effective in rural contexts.

The results have also shown that the extent of CE is different across interventions in both epidemiological contexts and socio-economic contexts. For instance in epidemiological contexts, although all interventions are more cost-effective in an LPC than they are in a HPC, PMTCT is comparably the most cost-effective, achieving a relative ICER of 56% in an LPC, while STD is comparably the least cost-effective, achieving an ICER of 97% in an LPC. In socio-economic contexts, not only do the CE trends depend on the intervention, the extent of CE is also different across interventions. For instance, the results indicate that HAART FOR ADULTS has the greatest extent of CE in the context in which it is more cost effective (ICER 151%).

The results in this chapter have shown that the CE of HIV/AIDS interventions is different across epidemiological contexts (an LPC and a HPC) and socio-economic contexts (a rural and an urban context). These results have provided ample evidence that the CE of HIV/AIDS interventions depends on the context, answering our research question on whether or not the CE of an HIV/AIDS intervention depends on the context and if so, to what extent. The results have indicated that CE and its extent indeed depend on the context and on the type of HIV/AIDS intervention.

Interpreting the meaning of these results requires reverting back to the methodology used in this analysis. The design of the analysis was such that there were different sizes of patient cohorts in different contexts, but the results presented were controlled for such differences. After controlling for the difference in the sizes in projections, the CE results would have been the same across contexts.

The fact that the results were not the same can be explained by the influence of the interaction between HIV/AIDS interventions and contextual and individual factors on the CE of HIV/AIDS interventions on the results. Theory has indicated that individual risk behaviours can be shaped by the context in which people live. Since these factors prevail to a different extent in different contexts and HIV/AIDS interventions do not necessarily target these factors, the outcomes of an intervention may be different.

On the basis of the above discussion, it can be concluded that CE depends on contexts and on the type of intervention. This conclusion implies that policy makers in South Africa need to consider how efficient HIV/AIDS interventions are in contexts in order to achieve more outcomes per health intervention.

Policy makers have been implementing HIV/AIDS interventions on the basis of factors other than contexts. This may have been due to the lack of evidence in this respect. CE studies conducted in South Africa compared CE across provinces and were conducted in the early 2000s. The most recent studies comparing CE in contexts were aimed at international policy makers. While the effects of context on the performance of interventions have been noted in the literature, they have not received sufficient attention in South Africa. Consequently, this analysis contributes to the literature on the CE of HIV/AIDS interventions in South Africa.

Although the findings of this study appear to be significant with respect to policy making in resource allocation, they need to be understood in the context of the evidence used in the analysis. While scenario analysis on the discount rates and the coverage of interventions did not seem to reveal a change in the conclusions of the base-case analysis, the conclusions were very sensitive to the cost assumptions. Given that the sources of estimates of the cost of the different interventions compared were inadequate, it is likely that the results might not be accurate. This calls for more studies on the cost analysis of health care interventions in general and HIV/AIDS interventions in particular, if policy on HIV/AIDS interventions is to be founded on solid evidence. Previous studies have also pointed to this need in Africa (see Creese *et al.*, 2002, for example).

Chapter summary

This chapter compared the CE of HIV/AIDS interventions in epidemiological and socio-economic contexts in South Africa. In epidemiological contexts, it was found that the effectiveness of HIV/AIDS interventions was greater in an LPC than in a HPC, while in socio-economic contexts, it was found that the effectiveness was lower in rural contexts than in urban contexts. The costs and CE patterns of HIV/AIDS interventions were different across contexts. The

findings suggest that policy makers in South Africa need to consider implementing HIV/AIDS interventions in line with the CE of such interventions in different contexts.

Chapter 10 : Summary, conclusions and recommendations

This chapter briefly recapitulates the work carried out in this study. Section one provides a summary of the research process, section two presents the main results and section three highlights the major conclusions of the study, while section four offers policy recommendations and suggests areas for further study.

10.1 Summary

This section summarises the research process. It recapitulates the objectives and rationale of the study as well as the research methods. The results and recommendations are presented in subsequent sections.

10.1.1 Objectives and rationale

This study set out to compare the CE of several HIV/AIDS interventions in epidemiological and socio-economic contexts in South Africa. In epidemiological settings, the study estimated and compared the CE of each of the modelled HIV/AIDS interventions in an LPC and in a HPC, while in socio-economic settings a similar comparison was done in a rural context and an urban context.

The comparison exercise was motivated by the multitude of factors influencing the impact of HIV/AIDS, assumed to exist to a different extent in each context. Since HIV/AIDS interventions do not necessarily target all these factors, the influence of these interventions on the impact of HIV/AIDS (effectiveness) was expected to be different from one context to another. Furthermore, the costs of HIV/AIDS interventions were expected to depend on contexts as the intensity and patterns of the interventions' activities and hence the resource requirements, were expected to follow the patterns and the extent of the impact of HIV/AIDS. A differentiated impact of HIV/AIDS in South Africa in the contexts of interest to this study (an LPC, a HPC, a rural context and an urban context) also motivated this research. Finally, the literature showing that the effectiveness of HIV/AIDS interventions depends on the context and that such

dependence should be considered by policy makers in implementing HIV/AIDS interventions (Grassly *et al.*, 2001; Vickerman *et al.*, 2006) was also inspiring.

A review of the literature revealed that only a few studies have compared the CE of HIV/AIDS interventions in contexts. Some studies have compared the CE of HIV/AIDS interventions across continents (Hogan *et al.*, 2005) or made comparisons between South Africa and other countries (Verguet & Walsh, 2010; Dowdy *et al.*, 2006). In South Africa, related but old evidence (Wilkinson *et al.* 2000) compared the CE of PMTCT across the country's nine provinces. Another South African study (Vickerman *et al.*, 2006) produced estimates on how to treat STD in patients with high risk behaviours and patients with low risk behaviours.

While related evidence has been available, it has mainly been of interest to international policy makers. Where it was directed at South African policy makers, it did not provide CE evidence in epidemiological and socio-economic contexts (areas) using a methodology that takes the interaction between interventions and contexts into account. By taking the gaps in the CE evidence for South Africa into account, this study has made a contribution to the body of knowledge in the area of the CE of HIV/AIDS interventions.

10.1.2 Methods

Three types of analysis were conducted. The first compared HIV/AIDS interventions across an LPC and a HPC using Markov modelling. The second compared the CE of HIV/AIDS interventions in a rural context and an urban context using Markov modelling. The third, using epidemiological projection models, compared the CE of HIV/AIDS interventions in an LPC and a HPC and then in a rural and an urban context.

The analysis in Chapter 7 compared the CE of an HIV/AIDS intervention across an LPC and a HPC without considering the CE of USUAL CARE for patients using that intervention. Markov states transition models as well as multidimensional measures of effectiveness (QALYs) were used. The size of the hypothetical cohort of patients (100,000 patients) was the same in each context and changed over time as a result of death. A detailed comparison of costs and effectiveness

was conducted in each HIV/AIDS state across contexts for each HIV/AIDS intervention. The overall cost and effectiveness of an HIV/AIDS intervention was also compared across contexts. The analysis was conducted over the lifetime of the patients in the cohort.

The analysis in Chapter 8 compared the CE of an HIV/AIDS intervention across a rural context and an urban context. The analysis took the cost and effectiveness of USUAL CARE for patients into account, using that intervention to capture the full effect of the interaction between contexts and HIV/AIDS interventions. Markov states transition models were used and the effectiveness was measured in terms of quality-adjusted life-years (QALYs). As in Chapter 7, a hypothetical cohort of the same size, 100,000 patients, was modelled in each context and for each intervention and the size of the cohort changed over time due to deaths. The ICER of each intervention relative to USUAL CARE was estimated in each context and the ICERs of a given intervention were compared in two contexts.

The analysis in Chapter 9 consisted of comparing the CE of HIV/AIDS interventions using a different modelling approach, epidemiological projection models, over the period 2007-2020. The ASSA2008 AIDS model (ASSA, 2011) and Spectrum Policy Modelling System (Stover, 2009) was used to estimate the effectiveness of an HIV/AIDS intervention in each context. These projections also enabled estimation of the costs of an HIV/AIDS intervention in each context on the basis of the projected or estimated number of annual patients for that intervention. As in Chapter 8, the estimation of the CE of an HIV/AIDS intervention took the cost and effectiveness of USUAL CARE into account in each context. Thus, the ICER of each intervention relative to USUAL CARE was estimated in each context and the ICERs of a given HIV/AIDS intervention were compared across two contexts. However, unlike in chapter 8, the sizes of patients modelled were assumed to be different across the contexts. These sizes changed over time as a result of migration, new births and deaths.

10.2 Results

This section summarises the results of the study. It presents the results in epidemiological contexts first and then in socio-economic contexts. In each set of contexts, the comparison of costs, effectiveness and CE results are distinguished.

10.2.1 Results in epidemiological contexts

Mixed patterns of the costs of HIV/AIDS interventions were obtained in epidemiological contexts. In an LPC, the average costs of STD and PMTCT were greater than they were in a HPC. In contrast, the average costs of VCT and HAART were less in an LPC than they were in a HPC (see Table 7:5). These mixed patterns of the costs across an LPC and a HPC were obtained when HIV/AIDS interventions were modelled with Markov models. When modelled with epidemiological projection models however, the incremental costs of each of the modelled HIV/AIDS interventions were greater in an LPC than they were in a HPC (see Table 9:1). The fact that the patterns of costs depended on the models used indicates the absence of a common pattern of costs of HIV/AIDS interventions across an LPC and a HPC.

Furthermore, the extent of the costs of a given HIV/AIDS intervention differed depending on the type of modelling and the type of interventions. Using Markov modelling, STD and PMTCT were more costly in an LPC than they were in a HPC. The average lifetime cost of STD and PMTCT in an LPC were 122% and 185% of their costs in a HPC, respectively. Using the same model however, the cost of VCT and HAART in a LPPC was lower than their cost in a HPC. These costs in an LPC were 76% and 14% of their costs in a HPC (see Table 7:5). Using epidemiological projection models however, the incremental costs per 100,000 patient-years of STD and PMTCT in an LPC were not relatively as high as in Markov modelling. These costs were 104% and 125% of their costs in a HPC (see Table 9:1). Using the same projection models, the incremental costs per 100,000 patient-years of VCT and HAART in an LPC were, in contrast to their costs with Markov modelling, greater than their costs in a HPC. These costs were 125% and 157% of their costs in a HPC (See Table 9:1). These results

show that the extent of the costs of modelled HIV/AIDS intervention not only depended on the context, but also on the modelling approach used and on the type of HIV/AIDS intervention. Hence, the need to pitch the modelling approaches against each other to establish which has greater value or credibility to facilitate choice.

While HIV/AIDS interventions did not display any pattern of costs across an LPC and a HPC, these interventions were consistently more effective in an LPC than they were in a HPC and this result prevailed regardless of whether Markov modelling or epidemiological projection models were used. However, even if HIV/AIDS interventions were more effective in an LPC than they were in a HPC, the extent of effectiveness differed across modelling approaches and across HIV/AIDS interventions.

To measure the extent of the effectiveness of an HIV/AIDS intervention in an LPC, the effectiveness in an LPC and in a HPC were compared. Specifically, the effectiveness of an HIV/AIDS intervention in an LPC was expressed as a percentage of its effectiveness in a HPC. A percentage of 100% implied that an HIV/AIDS intervention was equally effective across an LPC and a HPC, while a percentage above 100% meant that HIV/AIDS intervention was more effective in an LPC. This measure showed that the extent of effectiveness of these interventions varied across contexts.

The comparison of effectiveness of HIV/AIDS interventions across an LPC and a HPC revealed that the effectiveness of each HIV/AIDS intervention in an LPC, as a percentage of its effectiveness in a HPC, was greater than 100% (see Tables 7:6 and 9:2), regardless of the modelling approach used. Using Markov modelling, the incremental effectiveness of HIV/AIDS interventions in an LPC as a percentage of the effectiveness of HIV/AIDS interventions in a HPC ranged from 125% to 300% (see Table 7:6). Using epidemiological projection models, it ranged from 102% to 121% (see Table 9:2). Although a greater extent of effectiveness of HIV/AIDS interventions in an LPC was observed in Markov modelling, the pattern of effectiveness of HIV/AIDS interventions was such that more effectiveness was found in an LPC. These results meant that each of the

HIV/AIDS interventions modelled was more effective in an LPC than it was in a HPC.

The CE results which combined the results on costs and effectiveness showed that the CE of HIV/AIDS interventions was greater in an LPC. Having defined CE as the cost per health outcome and a more cost-effective intervention as one with lower costs per health outcome, the results of this study showed that each of the modelled HIV/AIDS interventions was more cost-effective in an LPC than it was in a HPC, regardless of the modelling approach (see Tables 7:7 & Table 9:3). These results suggested that the CE of HIV/AIDS interventions depended on the context.

Another observed result was the extent of difference in CE across HIV/AIDS interventions. Some HIV/AIDS interventions were most cost-effective than others in a given context. For instance, PMTCT was the most cost-effective in an LPC (on the basis that the CE of this intervention in an LPC as a percentage of its CE in a HPC is farthest from 100% regardless of the modelling approach), while STD was the least cost-effective in an LPC (see Table 7:8 & Table 9:4).

10.2.2 Results in socio-economic contexts

As in epidemiological contexts, mixed results with respect to the pattern of costs of modelled HIV/AIDS interventions were obtained in socio-economic contexts. HAART FOR ADULTS and HAART FOR CHILDREN were more costly in the rural context than they were in the urban context. Using Markov modelling, the incremental cost per 100,000 patient-years in a rural context for HAART FOR ADULTS and HAART FOR CHILDREN were 107% and 179%, respectively, of their incremental costs in the urban context (Table 8:5). When modelled with projection models the incremental costs per 100,000 patient-years in a rural context as a percentage of the incremental costs in an urban context were 143% and 103% (see Table 9:8). These results showed an absence of common patterns of costs across an LPC and a HPC for modelled interventions in socio-economic contexts.

Furthermore, the modelling revealed no common pattern of the extent of the costs of a given intervention. It was found that there was greater variation in costs across a rural and an urban context with Markov models than with projection models. The costs of HIV/AIDS interventions from any socio-economic context to another ranged from 29% to 179% with Markov models (see Table 8:5) and from 67% to 143% with projection models (see Table 9:8)²⁴.

While the costs of HIV/AIDS showed no common pattern across a rural context and an urban context, modelled HIV/AIDS interventions were consistently less effective in a rural context than they were in an urban context; this was consistent regardless of whether Markov modelling or epidemiological projection models were used (see Tables 8:4 and 9:10). However, as observed in epidemiological contexts, the extent of effectiveness differed across modelling approaches and across HIV/AIDS interventions.

HIV/AIDS interventions were more effective with Markov modelling than they were with epidemiological projection models. Using Markov modelling, the incremental effectiveness of HIV/AIDS interventions in a rural context as a percentage of the effectiveness of HIV/AIDS interventions in an urban context ranged from 53% to 86% (see Table 8:5). Using epidemiological projection models, it ranged from 65% to 91% (see Table 9:10). These results suggested that although the extent of effectiveness of HIV/AIDS interventions in a rural context was lower with Markov models compared with epidemiological models, the modelled HIV/AIDS interventions were generally less effective in a rural context than they were in an urban context regardless of the modelling approach used.

Taking into consideration cost and effectiveness, the results were such that there was no specific trend in the CE of HIV/AIDS interventions across a rural and an urban context. PMTCT was more cost-effective in the rural context than it was in the urban context while HAART FOR ADULTS and HAART FOR CHILDREN were more cost-effective in the urban context than they were in the rural

²⁴ Relative numbers (percentages) are used rather than absolute numbers to emphasize the relative comparability of HIV/AIDS interventions across contexts. This summary refers the reader to the full results in the main text of the thesis.

context. These results remained true regardless of the modelling approach used (see Table 8:4 & Table 9:11). The results showed that the CE of HIV/AIDS interventions depended on the context.

In addition to the absence of specific trends of CE across contexts, there was also a different extent of CE across HIV/AIDS interventions. Some HIV/AIDS interventions were most cost-effective in some contexts, whilst others were least cost-effective. PMTCT was the most cost-effective in a rural context (the ICER of PMTCT in a rural context as a percentage of its ICER in an urban context was farther away from 100%), while HAART FOR ADULTS was the least cost-effective in a rural context (see Table 9:12).

10.3 Conclusion and recommendations

This section provides the conclusion reached by this research study and responds to the research problem. It also makes some recommendations. It starts with the conclusion on the comparability of the costs, effectiveness and cost-effectiveness of modelled HIV/AIDS interventions and proceeds to provide recommendations.

10.3.1 Conclusion

This study aimed to determine whether or not the CE of HIV/AIDS interventions depends on the contexts of their implementation. On the basis of the results presented above, it is concluded that the CE of modelled HIV/AIDS interventions depends on the epidemiological contexts and socio-economic contexts where they are implemented. It is further concluded that the extent of CE is different across HIV/AIDS interventions. These results remained consistent regardless of the modelling approach used, although Markov modelling tended to increase the extent of the relative CE across HIV/AIDS interventions.

10.3.1.1 Conclusion for epidemiological contexts

In epidemiological contexts, after controlling for the size of the patient population, modelled HIV/AIDS interventions in South Africa were generally more costly in an LPC than they were in a HPC. However, the extent of relative

costs depended on the type of modelling used and on the type of HIV/AIDS intervention.

In epidemiological contexts, modelled HIV/AIDS interventions were generally more effective in an LPC than they were in a HPC although the extent of such effectiveness was different across HIV/AIDS interventions and depended on the type of modelling. Markov modelling made HIV/AIDS interventions more effective in an LPC than the results of projection models.

In epidemiological contexts, modelled HIV/AIDS interventions were generally more cost-effective in an LPC than they were in a HPC.

10.3.1.1 Conclusion for socio-economic contexts

In socio-economic contexts, there was no trend in the costs of HIV/AIDS interventions. The costs of some modelled HIV/AIDS interventions were greater in the urban context while the cost of other modelled HIV/AIDS interventions were lower in the urban context than they were in the rural context.

In socio-economic contexts, modelled HIV/AIDS interventions were generally more effective in urban contexts. In these contexts, the extent of effectiveness also differed across interventions and depended on the type of modelling used. Markov modelling made HIV/AIDS interventions more effective in an urban context than projection model results.

In socio-economic contexts, the pattern in the CE of HIV/AIDS interventions across a rural and an urban context was not specific and depended on the type of intervention. Of the modelled HIV/AIDS interventions, PMTCT was the most cost-effective in the rural context while HAART interventions were generally the most cost-effective in the urban context.

These results provided some evidence on which to base the overall conclusion of the study. It is concluded that the CE of modelled HIV/AIDS interventions in South Africa depends on the epidemiological and socio-economic contexts of the country.

10.3.2 Recommendations

In light of the above conclusion on the dependence of the CE of HIV/AIDS interventions on contexts, policy makers can achieve more health outcomes by allocating resources according to the CE of HIV/AIDS interventions in different contexts. This recommendation is based purely on efficiency criteria. Since policy makers make decisions on the basis of many criteria, including ethics and equity considerations, taking this aspect into consideration could be very significant towards the improvement of HIV/AIDS outcomes in South Africa. The reallocation of resources to achieve efficiency would not aim to completely remove any HIV/AIDS intervention in any specific context, thus abiding by equity and ethical considerations.

Because resources are allocated on the basis of cost-effectiveness, the evidence provided in this study would help policy makers achieve better health outcomes with the available budget. In allocating resources to HIV/AIDS interventions, policy makers should take epidemiological and socio-economic contexts into consideration in line with the findings of this study.

This study was restricted to the CE of HIV/AIDS interventions in an LPC and a HPC and in rural and urban contexts. Other comparisons which could have been considered include the CE of HIV/AIDS interventions across a rural context and an LPC, for example. Time and space constraints did not allow for such comparisons, which could be the subject of future research. Future research is also needed to improve the quantity and quality of data for studies of this kind. This study mixed modelled data and some data collected in the literature. Such data cannot be expected to be accurate and more research, particularly on data collection for CE studies, is crucial for South Africa.

REFERENCES

- Abdool Karim, Q.A. & Lawn, S.D. (2009). HIV Infection and Tuberculosis in South Africa. An Urgent Need to Escalate the Public Health Response. *Lancet*, 12 (9693), 921-933.
- Abdool Karim, Q.A, Abdool Karim, S.S., Frohlich, J.A., Grobler, A.C., Baxter, C., Mansoor, L.E., Kharsany, A.B.M., Sibeko, S., Mlisana, K.P., Omar, Z., Gengiah, T.N., Maarschalk, S., Arutapan, N., Mlotshwa, M., Morris, L. & Taylor, D. (2010). The Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide for the Prevention of HIV Infection in Women. *Science*, 3 (329), 1168-1174.
- Abdool Karim, S.S, Naidoo, K., Grober, A., Padayachi, N., Nair, G., Preenaar, J., Friedland, G., El-Sadr, N. & Abdool Karim, Q.A (2009). Initiating ART during TB Treatment Significantly Increases Survival: Results of a Randomised Controlled Clinical Trial in TB/HIV Co-infected Patients in South Africa. Abstract presented at the 16th Conference on Retroviruses and Opportunistic Infections, Montreal, February 8-11.
- Actuarial Society of South Africa (ASSA). (2011). AIDS and Demographic Model of the Actuarial Society of South Africa, ASSA2008 full model. Accessed at www.actuarialsociety.org.za, on 20/11/2011
- Adam, M. A., & Johnson, L. F. (2009). Estimation of Adult Antiretroviral Treatment Coverage in South Africa. *South African Medical Journal*, 99, 661-667.
- Adimora, A.A. (2012). Social Determinants of HIV/AIDS. Power Point Presentation. Presented at the Second International Workshop on HIV & Women, 9-10 January, Bethesda, MD, USA.
- Airhihenbuwa, C. O. (2004). Culture and African Contexts of HIV/AIDS Prevention, Care and Support. *Journal of Social Aspects of HIV/AIDS Research Alliance*, 1(1), 4-13.
- Ajzen, I. (1991). Theory of Planned Behaviour. *Organisational Behavior and Human Decision Process*, 50, 179-211.
- Alistar, S. S. & Brandeau, M. R. (2010). Decision Making for HIV Prevention and Treatment Scale-up: Bridging the Gap between Theory and Practice, *Medical Decision Making*, 32 (1), 105-117.
- Anderson, B.A.& Phillips, H. (2006). *Adult Mortality (age 16-64): Based on Death Notification Data in South Africa, 1997-2004*. Pretoria. Statistics South Africa.

- Anema, A., Au-Yeung, C.G., Joffres, M., Kaida, A., Vasarhelyi, K., Kanter, S., Montaner, J.S. & Hogg, R.S. (2011). Estimating the Impact of Expanded Access to Antiretroviral Therapy on Maternal, Paternal and Double Orphans in Sub-Saharan Africa, 2009-2020. *AIDS Research and Therapy* 8:13. Accessed at <http://www.aidsresearchtherapy.com/content/8/1/13> on 10/01/2013
- Arndt, C. & Lewis, J.D. (2001). The HIV/AIDS Pandemic in South Africa: Sectoral Impacts and Unemployment. *Journal of International Development*, 13(4), 427-449.
- Attia, S., Egger, M., & Muller, M. (2009). Sexual Transmission of HIV according to Viral Load and Antiretroviral Therapy: Systematic Review and Meta-Analysis. *AIDS*, 23, 1397-1404.
- Auvert, B., Males, S., Puren, A., Taljaard, D., Carael, M. & Williams, B. (2004). Can Highly Active Antiretroviral Therapy Reduce the Spread of HIV? A Study in a Township of South Africa. *Journal of Acquired Immune Deficiency Syndrome*, 36, 613-621.
- Auvert, A., Taljaard, D., Lagarde, E., Sobnoqui-Tambekou, J., Sitta, R. & Puren, A. (2005). Randomised Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infections Risk: The ANRS 1265 Trial. *Public Library of Sciences and Medicine*, 2 e298. Accessed at www.plosmedicine.org/article/info%3Ado%2F10.1371%2Fjournal.pmed.0020298, on 15/01/2012.
- Auvert, B., Ballard, R., Campbell, C., Carael, M., Carton, M., Fehler, G., Gouws, E., MacPhail, C., Taljaard, D., VanDam, J., Williams, B. (2001). HIV Infection among Youth in South Africa Mining Town is Associated with Herpes Simplex Virus-2 Seropositivity and Sexual Behaviour. *AIDS*, 15, 5885-5998.
- Babigumira, J.B., Castelnuovo, B., Lamorde, M., Kambugu, A., Stergachis, A., Easterbrook, P., Garrison, L.P. (2009). Potential Impact of Task-shifting on Costs of Antiretroviral Therapy and Physician Supply in Uganda. *Health services Research*, 9, 192-196. Accessed at www.biomedcentral.com/1472-6963/9/192#, on 10/01/2011.
- Bachmann, M. O. (2006). Effectiveness and Cost Effectiveness of Early and Late Prevention of HIV/AIDS Progression with Antiretrovirals or Antibiotics in Southern African Adults. *AIDS Care*, 18(2), 109-120.
- Bachmann, M. O., & Booyseen, F. L. R. (2003). Health and Economic Impact of HIV/AIDS on South African Households: a Cohort Study. *Biomedical Central Public Health*, 1-8. Published online. Doi: 10.1186/14712458314. Accessed at www.ncbi.nlm.nih.gov/pmc/articles/pmc155544, on 05/02/2010.
- Bachmann, M. O. & Booyseen, F. L. R. (2004). Relationship between HIV/AIDS, Income & Expenditure over Time in Deprived South African Households. *AIDS Care*, 16(7), 817-826.

- Badri, M., Clealry, S., Maartens, G., Pitt, J., Bekker, L.G., Orell, C. & Wood, R. (2006). When to Initiate Higly Active Antiretroviral Therapy in Sub-Saharan Africa? A South African Cost-effectiveness Study. *Antivil Therapy*, 11(1), 63-72.
- Badri, M., Maartens, G. & Mandalia, S. (2006). Cost-effectiveness of Highly Active Antiretroviral Therapy in South Africa. *Public Library of Sceince Medecine*, accessed at <http://www.ncbi.nlm.nih.gov/pubmed/16318413> on 20/06/2012.,
- Bandura, A. (1986). *Social Foundations of Thought and Action:A Social CognitiveTheory*. Englewood Clifffs, N J, Prentice Hall.
- Bangsberg, D.R., Perry, S., Charlebois, E.D., Clark, R.A., Robertson, M., Zolopa, A.R., Moss, A. (2001). Non-adherence to Highly Active Antiretroviral Predicts Progression to AIDS. *AIDS*, 15(9), 1181-1183
- Becker, M. H. (1974). *The Health Belief Model and Personal Health Behaviour*. . Michigan. Slack Inc.
- Becker, G. (1976). *The Economic Approach to Human Behavior*. Chicago, University of Chicago Press.
- Bedimo, A. L., Pinkerton , S. & Cohen, D. (2002). Condom Distribution: A Cost-effectiveness Analysis. *International Journal of STD and AIDS*, 13, 384-392.
- Bendavid, E., Young, S.D., Katzenstein, D.A., Bayoumi, A.M., Sanders,G.D. & Owen, D.K. (2008). Cost-effectiveness of HIV Monitoring Strategies in Resources Limited Countries: A Southern African Analysis. *Archives of Internal Medicine*, 168 (17), 1910-1918.
- Bhagwanjee, A., Petersen, I., Akinola, O., George, G. (2008). Bridging the Gap Between VCT and HIV Treatment Uptake: Perspective from a Mining-sector Workplace in South Africa. *African Journal of AIDS Research*, 7(3), 271-273.
- Bhattacharya, C., Bunzel, H., & Qiao, X. (2007). Unsafe Sex, AIDS and Development, *Staff General Research Papers*, No. 12832, Department of Economics, Iowa State University.
- Binagwaho, A., Peggurri, E., Muitta, J. & Bertozzi, S. (2010). Male Circumcision at Different Ages in Rwanda: A Cost Effectiveness Study. *Public Library of Science Medicine*. Accessed at <http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1000211> , on 10/10/2012.
- Bollinger L. and Stover J. (1999). *The Economic Impact of AIDS in Zambia*, The Futures Group International.
- Bolton, S. & Talman, A. (2010). *Interaction between HIV/AIDS and the Environment. A review of the Evidence and Recommendation for the Next Steps*. Report commissioned by IUCN_ESARO & IPPF-ARO, Nairobi.

- Bonell, C. & Imrie, J. (2001). Behavioral Interventions to Prevent HIV Infections: Rapid Evolution, Increasing Rigour, Moderate Success. *British Medical Bulletin*, 58, 155-170.
- Booyesen, F.L.R., Bachmann, M. O., Matebesi, Z. & Meyer, J. (2004). *The Socio-Economic Impact of HIV/AIDS on Households in South Africa: Pilot Study in Welkom and QwaQwa, Free State Province Final Report*. University of the Free State. Centre for Health Systems Research & Development.
- Bouare, O. (2009). Modelling Contextual Determinants of HIV/AIDS Prevalence in South Africa to Inform Policy. *African Journal of Reproductive Health*, 13 (3), 53-69.
- Boulle, A., Kenyon, C., Skordis, J. & Wood, R. (2002). Exploring the Costs of a Limited Public Sector Antiretroviral Treatment Programme in South Africa. *South African Medical Journal*, 92, 811-817.
- Bowden, W.P., Rhodes, S.D. & Jolly, C.P. (2006). Socio-cultural Determinants HIV/AIDS Risk and Services Use among Immigrant Latinos in North Carolina. *Hispanic Journal of Behavioral Sciences*, 28 (4), 546-562.
- Briggs, A. & Sculpher, M. (1998). An introduction to Markov Modelling for Economic Evaluation. *Pharmacoeconomics*, 13(4), 397-409.
- Business Report. (2012). South Africa to invest R1bn in ARV plant. Retrieved from www.iol.co.za, on 15/11/2012.
- CADRE. (2001). *HIV/AIDS and the Media: A Literature Review*. Report Accessed at http://www.cadre.org.za/files/LITREV_media_and_HIV/AIDS.pdf , on 15/02/2012.
- Caldwell, J. C. (2000). Rethinking the African AIDS Epidemic. *Population and Development Review*, 26(1), 117-135.
- Callaghan, M., Ford, N., and Schneider, H. (2010). A systematic review of task-shifting for HIV treatment and care in Africa. *Human Resources for Health*. 2010; 8: 8. Published online 2010 March 31. doi: 10.1186/1478-4491-8-8
- Campbell, C., Foulis, C.A., Maimane, S. & Sibiya, Z.I. (2005). I Have an Evil Child at my House: Stigma and HIV/AIDS Management in South African Community. *American Journal of Public Health*, 95, 808-815.
- Canning, D. (2006). The Economics of HIV/AIDS in Low-income Countries : The Case for Prevention. *Journal of Economic Perspectives*, 20(3), 121-142.
- Casale, M. & Whiteside, A. (2006). The Impact of HIV/AIDS on Poverty, Inequality and Economic Growth. *IDR Working Paper no 3 on Globalisation, Growth and Poverty*. International Development Research Centre, Ottawa.

- Case, A., Garrib, A., Menendez, A. & Olgiatti, A. (2008). Paying the Piper: the High Cost of Funeral in South Africa. NBER Working paper no 14456.
- Chancellor, J. V., Hill, A. M., Sabin, C. A., Simpson, K. N. & Youle, M. (1997). Modelling the Cost-Effectiveness of Lamivudine/Zidovudine Combination Therapy in HIV Infection. *Pharmacoeconomics*, 12, 1-13.
- Chigwedere, P., Seage, G. R., Gruskin, S., Lee, T. H. & Essex, M. (2008). Estimating the Lost Benefits of Antiretroviral Drug Use in South Africa. *Journal of Acquired Immune Deficiency Syndrome*, 49(4), 410- 415.
- Christofides, N., Muirhead, D., Jewkes, R. & Penn-Kekana, L. (2006). Including Post-exposure Prophylaxis to Prevent HIV and AIDS into Post-Sexual Assault Health Services in South Africa: Cost and Cost-effectiveness of User Preferred Approach to Provision. Accessed at <http://support.microsfot.com/kb/2123563>, on 15/05/2012.
- Chung, J., O'Brien, M., Price, J. & Shumbusho, F. (2008). Quantification of Physician time Saved in a Task Shifting Pilot Program in Rwanda. *AIDS 2008 – XVII International AIDS Conference. Abstract No WEAB0205*.
- Church, K. & Mayhew, S. H. (2009). Integrating STI and HIV Prevention, Care and Treatment into Family Planning Services: A Review of the Literature. *Studies in Family Planning*, 40 (3), 171-186.
- Cleary, S.M., Boulle, A., McIntyre, D., & Coetzee, D. (2004). Cost-effectiveness for Antiretroviral Treatment for HIV-Positive Adults in a South African Township. Report. Accessed at www.hst.org on 15/01/2011.
- Cleary, S. M., McIntyre, D. & Boulle, A. M. (2006). The Cost-Effectiveness of Antiretroviral Treatment in Kyayelitsha, South Africa, A Primary Data Analysis. *Cost-effectiveness and Resource Allocation*, 4 (20), 1-14.
- Cleary, S. M., McIntyre, D. & Boulle, A. M. (2008). Assessing Efficiency and Costs of Scaling up HIV Treatment. *AIDS*, 22 (Suppl 1), S35-S42.
- Coetzee, D., Hilderbrand, K., Goemaere, E., Matlatsi, F. & Boelaert, M. (2004). Integrating Tuberculosis and HIV Care in the Primary Setting in South Africa. *Topical Medicine and International Health*, 9(6), A11-A15.
- Cogneau, D & Grimm, M. (2006). Socio-economic Status, Sexual Behavior and Differential AIDS Mortality. *Population Research Policy Review*, 25, 393-407.
- Cohen, D.A., Wu, S.Y. & Farley, T.A. (2004). Comparing the Cost-effectiveness of HIV Prevention Interventions. *Journal of Acquired Immune Deficiency Syndrome*, 37,1404-1414.
- Collins, D. L. & Leibbrandt, M. (2007). The Financial Impact of HIV/AIDS on Poor Households in South Africa. *AIDS*, 21 (Suppl 7), S71-S81.

- Connolly, M.A., Gayer, M., Ryan, M.J., Salama, P., Spiegel, P., & Heymann, D.L. (2004). Communicable Diseases in Complex Emergencies: Impact and Challenges. *Lancet*, 364, 1974-1983.
- Creese, A., Floyd, K., Alban, A., & Guinness, L. (2002). Cost-effectiveness of HIV/AIDS Interventions in Africa: A Systematic Review of the Evidence. *Lancet*, 359, 1635-1642.
- Culliman, K. & Bodibe, K. (2010). Country Launches Massive HIV Testing Campaign. *Health-e*, April 2010.
- Dabis, J.F., Msilati, P., Meda, N., Weffens-Ekra, C., You, B., Manigart, O. & Leroy, V. (1999). Six-month-efficacy, Tolerance and Acceptability of a Short Regimen of Oral Zidovudine to Reduce Vertical Transmission of HIV/AIDS in Breastfed Children in Cote d'Ivoire and Burkina-Faso: A Double Blind Placebo Controlled Multi-centre Trial. *Lancet*, 353, 786-792.
- Dandona, L., Kumar, P., Ramesh, Y.K., Rao, M.C., Kumar, A.A., Marseille, E., Kahn, J. & Dandona, R. (2008). Changing Costs of HIV/AIDS Interventions in the Context of Scaling up. *AIDS*, 3 (Suppl 1), S43-S49.
- DeKoker, P., Lefevre, P., Matthys, F., Stuyft, P. & Delva, W. (2010). Barriers to Voluntary Counselling despite 13 Years of Community-based Awareness in a Peri-urban Township in Northern Limpopo. Scientific letter. *South African Medical Journal*, 100(6), 364-365.
- Department of Health. (2000). HIV/AIDS/STD Strategic Plan for South Africa 2000-2005. Accessed at <http://www.info.gov.za>, on 12/01/2011.
- Department of Health. (2003 a). Operational Plan for Comprehensive HIV and AIDS Care, Management and Treatment for South Africa. 2003. Accessed at <http://www.info.gov.za/issues/hiv/careplan.htm>, on 13/06/2011.
- Department of Health. (2003 b). *National HIV and Syphilis Antenatal Sero-Prevalence Survey in South Africa 2002*. Directorate of Health Systems Research, Research Coordination and Epidemiology. Pretoria.
- Department of Health. (2003 c). Demographic and Health Survey. Accessed at www.info.gov.za/view/DownloadFileAction?id=90143 , 08/04/2011.
- Department of Health. (2006). *Broad Framework for HIV & AIDS and Strategic Plan for South Africa, 2007-2011*. Accessed at <http://www.info.gov.za>, on 12/01/2010.
- Department of Health. (2010 a). *National Antenatal Sentinel HIV and Syphilis Survey in South Africa, 2009*. Pretoria.
- Department of Health. (2010 b). *Country Progress Report on the Declaration of Commitment on HIV/AIDS. 2010 Report*. Pretoria. Accessed at <http://www.zero-hic.co.za> , on 10/01/2012.

- Department of Health. (2010 c). *National PMTCT Accelerated Plan (A-Plan) Status Report*. Government Printers. Pretoria.
- Department of Health/ South African National AIDS Council. (2011). *National Strategic Plan on HIV, STI and TB 2012-2016*. Accessed at <http://www.sanac.org.za>, on 12/09/2012.
- Desmond, C. & Boyce, G. (2004). *Assessing the Rural PMTCT Pilot Site in the Eastern Cape*. Pretoria, HSRC.
- DiClemente, R.J., Crosby, R.A., Kegler, M.C. (2002). *Emerging Theories in Health Promotion Practice and Research*. Second Edition. Jossey-Bass. San Francisco
- Doherty, J. (2010). Cost-effectiveness Analysis for Priority Setting in South Africa-What Are the Possibilities? *South African Medical Journal*, 100, 816-821.
- Dolan, P. (1997). Modelling Valuations for EuroQol Health States. *Medical Care*, 35, 1095-1108.
- Dolan, P., Gudex, C., Kind, P. & Williams, A. (1995). A Social Tariff for Euroqol: Result from UK General Population Survey. *Discussion Paper 138* Department of Economics. University of New Castle-Upon -Tyne.
- Dorrington, R. (2011). Expansion of ARV Programme in SA Slows AIDS Mortality Rate. Media Release. *New Brief. info@fanews.co.za*. 9 March 2011. Actuarial Society of South Africa.
- Dowdy, D.W., Sweat, M.D. & Holtgrave, D.R. (2006). Country-wide Distribution of Nitrile Female Condom (FC2) in Brazil and South Africa: a Cost-effectiveness Analysis. *AIDS*, 20(16), 2091-2098.
- Drummond, M. F., Sculper, M. J., Torrance, G., O'Brien, B. & Stoddant, G. L. (2005). *Methods for the Economic Evaluation of Health Care Programmes*. Third Edition. Oxford. Oxford University Press.
- Egger, M., May, M., Chene, G. & Phillips, A. A. (2002). Prognosis of HIV-1 Infected Patients Starting Highly Active Antiretroviral Therapy: A Collaborative Analysis of Prospective Studies. *Lancet*, 360 (9327), 119-129.
- Ekman, B., Pathmanathan, I. & Liljestrang, J. (2008). Integrating Health Interventions for Women, Newborn Babies and Children: A Framework for Action. *Lancet*, 372, 990-1000.
- Euroqol Group. (1990). Euroqol-A New Facility for Measurement of Health Related Quality of Life. *Health Policy*, 16, 199-208.

- Fairall L R., Bachmann, O.& Louwagie, G.M. C. (2008). Effectiveness of Antiretroviral Treatment in a South African Programme. *Archives of Internal Medicine*, 168 (1), 86-93.
- Fassin, D. & Schneider, H. (2003). The Politics of AIDS in South Africa : Beyond the Controversies. *Biomedical Journal*, 326, 495-497.
- Ferrer, E., Santamarina, E., Domingo, P., Fumero, E., Ribera, E. Knobel, H. & Podzamcer, D. (2004). Nevirapine Containing Regimen in HIV Infected Naïve Patients with CD4 Cell Count of 200cells/ml or less. *AIDS*, 18, 1727-1740.
- Ferry, B., Caraeil, M., Buve, A. & Laourou, M. (2001). Comparison of Key Parameters of Sexual Behaviours in Four African Urban Population with Different Levels of Infections. *AIDS*, 5 (Supl 4), S41-S60.
- Fishbein, M. & Azjen, I. (1975). *Belief , Attitude, Intention and Behavior: An Introduction to Theory and Research Reading*. Chicago. Addison-Wesley.
- Fishbein, M., Bandura, A., Triandis, H. C., Becker, M. H. & Middlestadt, S. E. (1991). *Factors Influencing Behaviour and Behaviour Change. Final Report*. Theorist' Workshop Washington, October 3-5.
- Fisher, J.D., Fisher, W.A, Williams, S.S. & Malloy, T.E. (1994). Empirical Test of an Information-motivation-behavioral Skills Model of AIDS Preventive Behaviour with Gaymen and Heterosexual University Students. *Health Psychology*, 13, 238-250.
- Fisher J.D. & Fisher, W.A. (1992). Changing AIDS Risk Behavior. *Psychological Bulletin*, 111, 455-474.
- Floyd, K., Wilkinson, D., Gilks, C. (1997). Comparison of Cost-effectiveness of Directly Observed Treatment (DOT) and Conventionally Delivered Treatment for Tuberculosis: Experience from Rural South Africa. *Biomedical Journal*, 315 (7120), 1407-1411.
- Freedberg, K. A., Scharfstein, J. A., Seage, G. R., Losina, E., Weinstein, M. C. & Craven, D. E. (2001). The Cost-effectiveness of Combination of Antiretroviral Therapy for HIV Disease. *New England Journal of Medicine*, 344 (11), 824-831.
- Freire, S. (2004). Impact of HIV/AIDS on Saving Behaviour in South Africa. Africa Development and Poverty Reduction. The Macro-micro Linkages. Forum Paper DPRU/TIPS.
- Galaraga, O., Colchero, M.A., Wamai, R.G., Bertozzi, S.M. (2009). HIV Prevention Cost-effectiveness: A Systematic Review. *MBC Public Health*. Published online. Accessed at www.biomedicalcentral.com/14712458/9/S1/S5, on 10/03/2011.

- Galaraga , O., Writz, V.J., Figueroan-Lara, A., Santa-Ana-Tellez, Y., Coulibaly, I., Viisainen, K., Medina-Lara, A. & Korenromp, E.L. (2011). Unit Cost of Delivery of Antiretroviral Treatment and Prevention of Mother-to- Child Transmission. A Systematic Review. *Pharmacoeconomics*, 29(7), 579-599.
- Gandhi, N. R., Moll, A., Sturm, A. N., Pawnski, R., Govender, T., Lalloo, U., Zeller, K., Andrews, J. & Friedland, G. (2006). Extensively Drug Resistant Tuberculosis as a Cause of Death in Patient Co-infected with Tuberculosis and HIV in Rural Area of South Africa. *Lancet*, 368(9547), 1575-1580.
- Geffen, N., Nattrass, N. & Raubenheimer, C. (2003). The Cost of HIV Prevention and Treatment Interventions in South Africa. *CSSR Working Paper No. 28* January.
- Geoffard, P. Y. & Phillipson, T. (1996). Rational Epidemics and Their Public Control. *International Economic Review*, 37 (3), 603-604.
- Gilson, L., Mkanje, R., Grosskurth, H., Mosha, F., Picard. J., Gavyole, A., Todd, J., Mayaud, P., Swai, R., Fransen, L., Mabey, D., Mills, A. & Haves, R. (1996). Cost-effectiveness of Improved Treatment Services for Sexually Transmitted Diseases in Preventing HIV-1 Infection in Mwanza Region, Tanzania. *Lancet*, 350 (9094), 1805-1809.
- Glanz, K., Lewis, F. M. & Rimer, B. K. (1990). *Health Behaviour and Health Education. Theory Research and Practice*. San Francisco: Jossey-Bass Publishers.
- Goga, A.E., Dinh, T.H.& Jackson, D.J for the SAMPTCTE study Group. (2010). *Evaluation of the Effectiveness of the National Prevention of Mother-to-Child Transimission (PMTCT) Measured at 6 Weeks Postpartum in South Africa*. South African Medical Research Council. Department of Health and PEPFAR/US Centre for Disease Prevention and Control.
- Gold, M. E., Siegel, J. E., Russel, L. B. & Weinstein, M. C. (1996). *Cost-effectiveness in Health and Medicine*. Oxford.Oxford University Press.
- Goldie, S., Yaznapnah, Y. & Losina, E. (2006). Clinical Benefits and Cost-Effectiveness of Antiretroviral Therapy for Human Immunodeficiency Virus-infected Patients in Resource-poor Settings: The Case of Cote d'Ivoire. *New England Journal of Medicine*, 355, 141-53.
- Gouws, E. (2010). HIV Incidence Rates in Sotuh Africa, in Abdool Karim, S.S.,& Abdool Karim, Q.A. (eds). *HIV/AIDS in South Africa*. Second edition, 74-84. Cambrige. Cambridge University Press
- Gouws, E. & Abdool Karim, Q. A. (2010). HIV Infection in South Africa: The Evolving Epidemic, in Abdool Karim, S.S & Abdool Karim, Q.A.(eds). *HIV/AIDS in South Africa*. Second edition pp 55-73. Cambridge. Cambridge University Press.

- Govender, K. (2011). OneLOve Campaign Making Strides. Buanews, 10 June.
- Govender, P. (2009). South Africa to Expand AIDS Treatment-Zuma. *Reuters December 1*. Accessed at <http://uk.reuters.com/article/2009/12/01>, on 10/01/2012.
- Govender, V., McIntyre, D., Grimwood, A. & Marteens, G. (2000). The Costs and Perceived Quality of Care for People Living with HIV/AIDS in Western Cape Province in South Africa. *Small Applied Research*, No 14, Bethesda.
- Granich, R., Kahn, J.G., Bennett, R., Holmes, C.B., Garg, N., Serenata, C., Sabin, M.L., Makhoulf-Obermeyer, C., Mack, C.D.F., Williams, P., Jones, L., Smyth, C., Kutch, K.A., Ying-Ru, L., Victoria, M., Souteyrand, Y., Crowley, S., Korenromp, E.L. & Williams, B.G. (2012). Expanding ART for Treatment and Prevention of HIV in South Africa: Estimated Costs and Cost-effectiveness 2011-2050. *Public Libray of Sciences One*. Accessed at <http://www.plosone.org/article/info:doi/10.1371/journal.pone.0030216> on 15/12/2012.
- Grassly, N. C., Garnett, G.P., Schwartlander, B., Gregson, S. & Anderson, R. M. (2001). The Effectiveness of HIV Prevention and the Epidemic Context. *Bulletin of the World Health Organisation*, 79(12), 1121-1132.
- Gray, R.H., Li, X, Kigozi, G., Serwadda, D., Nalugoda, F., Watya, S., Reynold, S.J. & Wawer, S.J. (2007). The Impact of Male Circumcision on HIV Incidence and Cost per Infection Prevented: A Stochastic Simulation Model from Rakai, Uganda. *AIDS*, 21 (7), 845-850.
- Griffiths, J.D., Lawson, Z.F., & Williams, J.E (2006). Modelling Treatment Effect in the HIV/AIDS Epidemic. *Journal of the Operational Research Society*, 57, 1413-1424.
- Guay, L. A., Musoke, P. & Fleming, T. (1999). Intrapartum and Neonatal Single-Dose Nevirapine Compared with Zidovudine for Prevention of Mother-to-Child Transmission of HIV-1 in Kampla, Uganda: HIVNET012 Randomised Trial. *Lancet*, 354, 795-802.
- Halett, T.B., Gregson,S., Lewis,J.J.C, et al., (2007). Behaviour change in generalised HIV epidemics: impact of reducing cross-generational sex and delaying age at sexual debut, *Sexually Transmitted Infections*, 83,I50-I54
- Harling, G., Bekker, L.G., & Wood, R. (2007). Costs of a Dedicated ART Clinic. *South African Medical Journal*, 97(8), 593-596.
- Harrison, A. (2010). Young People and HIV/AIDS in South Africa: Prevalence of Infections, Risk Factors and Social Contexts, in Abdool Karim, S.S. & Abdool Karim, Q.A. (eds). *HIV/AIDS in South Africa*, Second edition, pp325-345. Cambridge. Cambridge University Press.

- Harrison, A., Newel, M. L., Imrie, J. & Hoodinot, G. (2010). HIV Prevention for South African Youth: Which Interventions Work? A Systematic Review of Current Evidence. *Biomedical Public Health*, 26,10:102. Accessed at <http://www.ncbi.nlm.nih.gov/pubmed/20187957>, on 10/02/2012.
- Hausler, H.P., Sinanovic, E., Kumaranayake, L., Naidoo, P., Schoeman, H., Karpakis, B. & Godffrey-Fausset, P. (2006). Costs of Measures to Control Tuberculosis/ HIV in Public Primary Care Facilities in Cape Town, South African. *Bulletin of the World Health Organisation*, 84,528-536.
- Herbst, A. J., Cooke, G. S., Bärnighausen, T., KanyKany, A., Tanser, F., Newell, M. (2009). Adult Mortality and Antiretroviral Treatment Rollout in Rural KwaZulu-Natal, South Africa. *Bulletin of the World Health Organisation*, 87, 754-762.
- Hogan, D. R., Balthussen, R., Hayashi, C., Laurer, J. A. & Salomon, J. A. (2005). Cost-effectiveness Analysis of Strategies to Combat HIV/AIDS in Developing Countries. *Biomedical Journal*, 2, 123-135.
- Hogg, R.S., Weber, E. & Crab, K.J (1998). One World, One Hope, the Cost of Providing Antiretroviral Therapy to all Nations. *AIDS*, 12, 2203-2209.
- Hogg, R. S., Yip, B., Chan, K. J. & Wood, E. (2001). Rates of Disease Progression by Baseline CD4 Cell Count and Viral Load after Initiating Triple-drug Therapy. *Journal of the American Medical Association*, 286 (20), 2568- 2577.
- Holtgrave, D. R. & Kelly, J. A. (1996). Preventing HIV/AIDS among High-risk Urban Women: The Cost-effectiveness of Behavioural Group Interventions. *American Journal of Public Health*, 86, 1442-1445.
- Hontelez, J. A. C., Devias, S. J., Tanser, F., Bakker, R., Barnighuassen, T., Newell, M.L., Baltussen, R., & Lurie, M. (2011). The Impact of the New WHO Antiretroviral Treatment Guidelines on HIV Epidemic Dynamics and Cost in South Africa. *PlusOne*. Accessed at <http://www.plosone.org/article/info%3Adoi.1371%2Fjournal.pone.0021919>, on 06/08/2012
- Hoque, M., Hoque, E., Kader, S.B. (2008). Audit of Antinatal Care in a Rural District in KZN, South Africa. *South African Family Practice*, 50 (3), 66-72.
- Hsu, J., Zinsou, C., Parkhurst, J., N'Dour, M., Foyet, L. & Mueller, D.H. (2012). Comparative Costs and Cost-effectiveness of Behavioral Interventions as Part of HIV Prevention Strategies. *Health Policy and Planning*, 15:175-189
- HSRC/MRC/CADRE. (2005). *Nelson Mandela/HSRC Study of HIV/AIDS. South African National HIV prevalence, Incidence, Behaviour and Communication Survey 2005*. Cape Town: HSRC Press.
- HSRC/MRC/CADRE. (2009). *South African National HIV prevalence, Incidence, Behaviour and Communication Survey 2008. A Turning Tide among Teenager*. Cape Town: HSRC Press.

- HSRC/MRC/CADRE. (2013). *South African National HIV prevalence, Incidence, Behaviour and Communication Survey 2012. A Turning Tide among Teenagers*. Cape Town: HSRC Press.
- Hussain, A., Moodley, D., Naidoo, S. & Esterhuizen, T.M. (2011). Pregnant Women's Access to PMTCT and ART Services in South Africa and Implication for Universal Antiretroviral Treatment. *Plos One*. Accessed at www.plosone.org/article/info , on 10/01/2012.
- Hweshe, F. (2011). More to Benefit from Social Grants. Accessed at <http://www.southafrica.info/about/social/436302.htm>, on 06/07/2011.
- IRIN/Plus News. (2012). South Africa: Revamped AIDS Council Makes its Debut. October, 9. Johannesburg.
- Jackson, J. B. & Fleming, T. (2003). Intrapartum and Neonatal Single Dose Nevirapine Compared with Zidovudine for Prevention of Mother-to-Child Transmission of HIV-1 in Kampala, Uganda: 18-months of Follow-up of HIVNET012 Randomised Trial. *Lancet*, 362, 859-868.
- Jan, S., Ferrari, G., Watts, C.H., Hargreaves, J.R., Kim ,J.C., Phetla, G. & Pronyk, P.M. (2011). Economic Evaluation of Combined Microfinance and Gender Training Intervention for the Prevention of Intimate Partner Violence in South Africa. *Health Policy and Planning*, 26, 366-372.
- Jelsma, J., Maclean, E., Hughes, J., Tinise, X. & Darder, M. (2005). An Investigation into the Health-related Quality of Life of Individuals Living with HIV Who are Receiving HAART. *AIDS Care*, 17 (5), 579-588.
- John, F.N., Farquhar-Kiarie, J.N., Kabura, M.N. & John-Stewart, G.C. (2008). Cost Effectiveness of Couple Counseling to Enhance Infant HIV-1 Prevention. *International Journal of STDs and AIDS*, 19 (6), 406-409.
- Johnson, K. (2004). The Politics of AIDS Policy Development and Implimentation in Post Apartheid South Africa. *Africa Today*, 51 (2), 107-128.
- Johnson, L., Coetzee, D., & Dorrington, R.(2005). Sentinel Surveillance of Sexually Transmitted Infections in South Africa; A Review. *Sexually Transmitted Infections*, 8(4), 287-293.
- Johnson, L. F. & Dorrington, R. E. (2006). Modeling the Demographic Impact of HIV/AIDS in South Africa and the Likely Impact of Interventions. . *Demographic Research*, 14, 541-574.
- Johnson, L. F (2008). *The Interaction between HIV and Other Sexually Transmitted Infections in South Africa: A Model-based Evaluation*. PhD Thesis. University of Cape Town.
- Johnson, L. & Budlender, D. (2002). HIV Risk Factors:A Review of Demographic, Socio-economic, Biomedical and Behavioural Determinants of HIV

Prevalence in South Africa. Centre for Actuarial Research (CARE). University of Cape Town.

- Kagee, A. (2006). Adherence to Antiretroviral Therapy in the Context of the National Rollout in South Africa: Defining a Research Agenda for Psychology. *South African Journal of Psychology*, 38 (2), 413-428.
- Kahn, J. G., Mareseille, E. & Auvert, B. (2006). Cost-effectiveness of Male Circumcision for HIV Prevention in South African Setting. *Public Library of Science Medicine*, 3 (12), 2349-2358.
- Kahn, J.G. (1996). The cost-effectiveness of HIV Prevention Targeting: How much more Bangs for the Buck? *American Journal of Public Health*, 86 (12), 1709-1711.
- Kania, D., Sngare, L., Sakande, J., Koanda, A., Nebie, Y.k., Zerbo, O., Combassere, A.V., Guissou, I.P., Rouet, F.(2009). *A New Strategy to Improve the Cost-effectiveness of Human Immunodeficiency Virus, Hepatitis B Virus, Hepatitis C Virus, and Syphilis testing of Blood Donations in Sub Saharan Africa: A Pilot Study in Burkina-Fasso*. Brief Report accessed at http://www.securiserlefutur.com/publications/data/blood_safety.pdf, on 25/06/2011.
- Kalitchman, S.C & Simbayi, L.C. (2006). Association of Poverty, Substance Use, and HIV Transmission Risk Behaviors in Three South African Communities. *Social Science and Medicine*, 62(7), 1641-1649.
- Kelly, J. A., Lawrence, J. S., Diaz, Y. E., Stevenson, L.Y., Hauth, A.C., Brasfield, S.C. & Andrew, M.E. (1991). HIV Risk Behaviours Reductions Following Interventions with key Opinion Leaders of the Population. An Experimental Analysis. *American Journal of Public Health*, 81 (2), 168-171.
- Kleinschmidt, I., Pettifor, A., MacPhail, C., & Rees, H. (2007). Geographical Distribution of Human Immunodeficiency in South Africa. *American Journal of Tropical Medicine and Hygiene*, 77(6), 1163-1169
- Kenyon, C., Skordis, J., Boulle, A. & Pillay, K. (2003). The ART of Rationing-the Need for a New Approach to Rationing Health Interventions. *South African Medical Journal*, 93, 56-60.
- Kincaid, L & Coleman, P. (2006). South African HIV/AIDS Serial Drama helps Decrease Stigma and Improve Prevention Behaviours among the Youth. *Communication Impact*, 20, 1-10.
- Korenromp, E.L., White, R.G, Orroth, K.K., Bakker, R., Kamali, Serwadda, R., Gray, R.H., Groskurth, H., Habbema, J.D & Hayes, R. J. (2005). Determinants of the Impact of Sexually Transmitted Infections on Prevention of HIV Infections: A Synthesis of Evidence from Mwanza, Rakai, and Masaka Intervention Trials. *The Journal of Infectious Diseases*, 191 (Suppl 1), S168-S175.

- Laga, M., Schwartlander, B., Pisani, E., Sow, P.S. & Carael, M. (2001). To Stem HIV in Africa, Prevent HIV in Young Women. *AIDS*, 15(7), 931-934.
- Leach-Lemens, C. (2011). South Africa's PMTCT Programme Reduces Mother-to-Child Transmission to under 4.%. *AIDSMap*, 19 July. Accessed at <http://www.aidsmap.com/South-Africas-PMTCT-programme-reduces-mother-to-child-transmission-to-under-4/page/1880446/>, on 15/04/2012.
- Levy, A (2002), A Lifetime Portfolio of Risky and Risk-free Sexual Behaviour and the Prevalence of AIDS. *Journal of Health Economics*, 21(6), 993-1007.
- Long, L., Breannan, A., Fox, M.P., Ndibongo, B., Jaffray, I., Sanne, I. & Rosen, S. (2011). Treatment Outcomes and Cost-effectiveness of Shifting Management of Stable ART Patients to Nurses in South Africa: An Observational Cohort. *PloS Med*, 8 (7),: e1001055.doi:10.1371/journal.pmed.10001055. Accessed at www.plosmedicine.org/article/info%3Adol%2F10.1371/journal.pmed.10001055, on 10/02/2011.
- Louwagie, G.M., Meyer, K., Booysen, F. L. R., Fairal, L.R., Heunis, C. (2007). Highly Active Antiretroviral Treatment and Health related Quality of Life in South Africa Adults with Human Immunodeficiency Virus Infection. A Cross sectional Analytical Study. *BMC Public Health* online. Accessed at www.ncbi.nlm.nih.gov/pubmed/17854510, on 08/06/2011.
- Lucchini, S., Cisse, B., Duran, S., Decenival, M., Comiti, C., Gaudry, M., Moatti, J.P. (2007). Decrease in Prices of Antiretroviral Drugs for Developing Countries: from political "philanthropy to Regulated Markets. Available at <http://apps.who.int/medicinedocs/documents/s18253en/s18253en.pdf>, on 10/02/2013
- Mahajan, A.P., Sayles, J.N., Patel, V.N., Remien, N.H., Sawires, S.R., Ortiz, D.J., Szekeres, G. & Coates, T.J (2008). Stigma in HIV/AIDS Epidemic: A Review of the Literature and Recommendations for the Way Forward. *AIDS*, 22 (Suppl 2), S67-S79.
- Maharaj, P. & Cleland, J. (2005). Integratiion of Sexual and Reproductive Health Services in KwaZulu-Natal South Africa. *Health Policy and Planning*, 20 (5), 310-318.
- Mannak, M. (2009). Activists Lament Lack of HIV/TB Co-treatment. Inner Press Services 26 March, Cape Town. Accessed at <http://www.aegis.com/news/ips/2009/IP090314.html> , on 12/01/2010.
- Marseille, E., Kahn, J. G., Billinghamurst, K. & Saba, J. (2001). Cost-Effectiveness of Female Condom in Preventing HIV and STDs in Commercial Sex Workers in Rural South Africa. *Social Science and Medicine*, 52, 135-148.
- Marseille, E., Kahn, J. G. & Saba, J. (2001). Cost-effectiveness of Antiviral Drug Therapy to Reduce Mother-to-child HIV Transmission in Sub-Saharan Africa. *AIDS*, 12, 939-948.

- Marshall, B. D. L., Kerr, T., Shoveller, J. A., Montaner, J. S. G. & Wood, E. (2009). Structural Factors Associated With an Increased Risk of HIV and Sexually Transmitted Infection Transmission among Street Involved Youth. *Biomedical Central Public Health* 9(7). Accessed at www.biomedicalcentral.com, on 15/07/2011.
- Marmot, M. & Wilkinson, R. (2005). *Social Determinants of Health*. Oxford. Oxford University Press.
- Marseille, E., Hofman, P.B., Kahn, J.G. (2002). HIV prevention before HAART in Sub-Saharan Africa. *The Lancet*, 359, 1851-1856
- Martin, G., Bollinger, L., Pandit-Rajani T, et al. (2010). Costing Male Circumcision in Lesotho, Swaziland, and Zambia: Implications for the Cost-effectiveness Of Circumcision as an HIV Intervention. USAID; Washington DC: [accessed 10 May 2010]. 2007. tinyurl.com/circum-cost.
- Masobe, P., Lee, T., & Price, M. (1995). Isoniazid Prophylactic Therapy for Tuberculosis in HIV-seropositive Patients –A Least Cost Analysis. *South African Medical Journal*, 85, 75-84.
- Mathews, C. (2010). Reducing Sexual risk Behaviours: Theory and Research, in Abdool Karim, S.S., & Abdool Karim, Q.A. (eds). *HIV/AIDS in South Africa*. Second edition, 157-182. Cambridge. Cambridge University Press
- McConnel, C.E., Stanley, N., Duplessis, J.A., Pitter, C.S., Abdullah, F., Coovadia, H.M., Marseille, E & Kahan, K.G. (2005). The Cost of a Rapid VCT in South Africa. *South African Medical Journal*, 95 (12), 968-971.
- McGowan, J, P., Shah, S.S., Ganea, C.E., Blum, S., Ernst, J.E., Irwin, K & Weidle, P.J. (2004). Risk behavior for transmission of human immunodeficiency virus (HIV) among HIV-seropositive individuals in an urban setting. *CID*, 38(January), 122-127
- Mdege, N.D., Chindove, S. & Ali, S. (2012). The effectiveness and Cost Implications of Task-shifting in the Delivery of Antiretroviral Therapy to HIV-infected Patients: A Systematic Review. *Health Policy and Planning*, 2 1-14.
- Mekonnen, Y., Jegou, R., Coutinho, R., Anokos, J and Fontanet, A. (2011). Demographic Impact of AIDS in a Low-fertility Urban African Setting: Projection for Addis Ababa, Ethiopia. *Journal of Health, Population and Nutrition* 20(2):120-129
- Meldrum, A. (2006). South African Government Ends AIDS Denial. *The Guardian*, 28 October.
- Menzies, N.C., Beruti, A.A. & Blandford, J.M. (2012). The Determinants of HIV Treatment Costs in Resource Limited Settings. *Public Library of Science Medicine*. Accessed at www.plosone.org/article, on 06/09/2012.

- Meyer-Rath, G. (2007). The Cost-Effectiveness of HIV Control: Getting the Priorities Right. *Southern African Journal of HIV Medicine*, 8(2), 15-16.
- Meyer-Rath, G (2010). *The Cost of National Antiretroviral Treatment Program*. Health Economics and Epidemiological Research Office, Wits Health Consortium, Centre for Global Health and Development.
- Meyer-Rath, G; Miners, A., Santos , A.C., Variava E.& Venter ,W.D. (2012). Costs and Resources Uses of Patients on Antiretroviral Therapy in the Urban and Semi Urban Public Sectors of South Africa. *Journal of Acquired Immune Sysndrome*, 61(3):e25-32
- Meyer-Rath, G., Brennan, A, Long, L, Ndibongo, D, Technau, K., Moultrie, H., & Rosen, S. (2013). Cost and Outcomes of Paediatric Antiretroviral Treatment in South Africa. *AIDS*, 27 (2), 243-250.
- Meyer-Rath, G & Over, M.(2012). HIV Treatment and Prevention. Modelling the Cost of Antiretroviral Treatment-State of the Art and Future Directions.*Public Library of Science Medicine*. Accessed at <http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001247>, on 11/03/2013
- Meyers, T., Moultrie, H., Naidoo, K., Cotton, M., Eley, B.& Sherman, G. (2007). Challenges to Pediatric HIV Care and Treatment in South Africa. *Journal of Infectious Diseases*,196 (Supl.3), S474-S48.
- Mills, E. (2008): Swimming into Confusion: A Qualitative Study of Factors Affecting Uptake and Adherence to Antiretroviral Treatment in South Africa. *CSSR Working Paper No 208*.
- Motsoaledi, A. (2011). *How we are re-engaging the health System*. Health Budget Vote Policy Speech Presented at the National Assembly. Cape Town. South Africa.
- Moses, S., Plummer, F. A., Ngugi, E. N., Nagelkerke, N.J., Anzala, A.O., & Ndimya-Achola, J.O. (1991). Controlling HIV in Africa: Effectiveness and Costs of an Intervention in a High Frequency STD Transmitter Core Group. *AIDS*, 5(4), 407-411.
- Muennig, P. (2008). *Cost-effectiveness Analysis in Health, A Practical Approach*. Second edition. San Francisco. Jossey-Bass.
- Muirhead, D., Kumaranayake, L. & Watts, C. (2001). *Economically Evaluating the Soul City Series*. Report Prepared for Soul City Institute for Health and Development Communication.
- Munakata, J., Benner, J.S., Becker, S., Dezii, C.M., Hazard, E.H. & Tierce, J.C. (2006). Clinical and Economic Outcomes of Nonadherence to Highly Active Antiretroviral Therapy in Patients with the Human Immunodeficiency Virus. *Medical Care*, 44, 893-899.

- Muntinta, G., Gow, J., George, G. & Kunda, K. (2011). The Influence of Socio-Economic Determinants on HIV Prevalence in South Africa. *Review of Economics and Finance*, 3, 96-106.
- Naidu, V. & Harris, G. (2006). The Economic Impact of HIV/AIDS on Urban Households. *South African Journal of Economics*, 25 (3), 146-158.
- National HIV/AIDS & Tuberculosis Programme. (2003). Government Khomanani Campaign. *Newsletter No. 38*, 27 October.
- Nattrass, N. & Geffen, N. (2005). The Impact of Reduced Drug Prices on the Cost-effectiveness of HAART in South Africa. *African Journal of AIDS Research*, 4(1), 65-67.
- Ndlovu, N. (2009). *Review of South Africa's 2009 HIV/AIDS budgets: Quick update.*, Centre for Economic Governance and AIDS in Africa.
- Nicolosi, A., Correa leit, M.L., Musiccom, M., Aric, C., Gavazzeni, G. & Lazzarin, A. (1994). The Efficiency of Male-to-Female and Female-to-male Sexual Transmission of the Human Immunodeficiency Virus: A Study of 730 Stable Couples. *Epidemiology*, 5(6), 570-575.
- Nyabadza, F; Mukandavire, Z. & Hove-Musekwa, S.D. (2010). Modelling the HIV Trends in South Africa: Insights from a Simple Mathematical Model. *Non Linear Analysis: Real World Applications*, 12, 2091-2104.
- Obure, C.D., Vassal, A., Michael, C., Terris-Prestholt, F., Mayhew, S., Stachpool-Moore, L., Warren, C., Watts, C.(2012). Optimising the Cost and Delivery of HIV Counselling and Testing Services in Kenya and Swaziland. *Sexually Transmitted Infections*, 88(7), 498-503
- O'Donnell. M.R., Padayachi, N., Kvasnovsky, C, Werner, L., Master, I. & Horsburgh, R. (2013). Treatment Outcomes for Extensively Drug Resistant Tuberculosis and HIV Co-infection. *Emerging Infectious Diseases*, 19(3): 416-424.
- Ojteg, K. (2008). *Socio-economic Determinants of HIV in Zambia: A District Level Analysis*. School of Economics and Management. Lund University. Master's Thesis.
- O'Keefe, E. A., Wood, R. (1996). The Impact of Human Immunodeficiency Virus (HIV) Infection on Quality of Life in a Multiracial South African Population. *Quality of Life Research*, 5, 275-280.
- Oster, E. (2007). HIV and Sexual Behaviour Change: Why not Africa?, *NBER Working Paper*, No. 13049
- Parker, R. & Aggleton, P.(2002). *HIV/AIDS- related Stigma and Discrimination: A Conceptual Framework and Agenda for Action*. Geneva. UNAIDS.
- Parker, F.(2010). NHI will cost same as current healthcare, Mail & Guardian, 10 September 2010, <http://uct-heu.s3.amazonaws.com>.

- Parker, W. (2003). Re-appraising Youth Prevention in South Africa: The Case of Love life. *South African AIDS Conference in Durban*, August 2003.
- Peck, R., Fitzgerald, D.W., Liautaud, B., Deschamps, M.M., Verdier, R.I., Beaulieu, M.E., GrandPierre, R., Joseph, P., Severe, P., Noel, F., Wright, P., Johnson, Jr, W.D & Pape, J.W. (2003). The Feasibility, Demand, and Effects of Integrating Primary Care Services with HIV Voluntary Counselling and Testing. *Journal of Acquired Immune Deficiency Syndrome*, 33 (4), 471-475.
- Pelitzer, K., Matseke, G., Mzolo, T. & Mjaja, M. (2009). Determinants of Knowledge of HIV Status in South Africa: Results from a Population Based HIV Survey. *Biomedical Central Public Health*, 9, 174-174.
- Pelitzer, K., Mosala, T., Shisana, O. & Nqeteko, A. (2006). Utilization of Delivery Services in the Context of Prevention of HIV from Mother- to -child in a Rural Community, South Africa. *Curationis*, 29 (1), 54-64.
- Pendukeni, M (2004). The Impact of HIV/AIDS on the Health Care Provision: Perceptions of Nurses Currently Working in one Regional Hospital in Namibia. Masters Dissertation. University of Western Cape.
- Pettifor, A., Rees, H.V., Steffenson, A., Hlongwa- Madikizela, L., MacPhail, C., Vermaak, K. & Kleinschmidt, I. (2004). HIV and Sexual behaviours Among South African: A National Survey of 15-24 Year Old, Reproductive Research Unit. Accessed at <http://www.rhu.co.za/Downloads.asp>, on 15/01/2012.
- Philipson, T. & Posner, R. (1993). *Privates Choices and Public Health: The AIDS Epidemic in an Economic Perspective*. Cambridge. Havard University Press.
- Pitpitan, E.V., Kalichman, S.C., Eaton, L.A., Cain, D., Sikkema, K.J., Skinner, D., Watt, M.H. & Pieterse, D. (2012). AIDS-related Stigma, HIV Testing, and Transmission Risk among Patrons of Informal Drinking Places in Cape Town, South Africa. *Annals of Behavioural Medicines*, 43, 632-371.
- Pretorius, C., Stover, J., Bollinger, L., Bacaer, N. & Williams, B. (2010). Evaluating the Cost-effectiveness of Pre-exposure Prophylaxis and its Impact on HIV/AIDS Transmission in South Africa. *Public Library of Science One (PloS One)*, 5(11), 13646. doi:10.1371/journal.pone.0013646. Accessed at www.plosone.org/article/info, on 10/03/2012.
- Price, M.A., Stewart, S.R., Miller, W. C., Behets, F., Dow, W.H., Martinson F.E., Chilongozi, D. & Cohen, M.S. (2006). The Cost-effectiveness of Treating Male Trichomoniasis to Avert HIV Transmission in Men Seeking Sexually Transmitted Disease Care in Malawi. *Journal of Acquired Immune Deficiency Syndrome*, 43(2), 202-209

- Pronyk, P. M., Kim, J. C., Abramsky, T., Phetla, G., Hargreaves, J., Morrisson, L., Watts, C., Busza, J. & Porter, J. D. (2008). Combined Microfinance and Training Interventions Can Reduce HIV Risk Behaviour in Young Female Participants, *AIDS*, 22, 1659-1666.
- Pronyk, P., Hargreaves, J., Kim, J. C., Morrisson, L. A., Phetla, G., Watts, C., Busza, J. & Porter, J. D. (2006). Effects of Structural Intervention for the Prevention of Intimate Partner Violence and HIV in Rural South Africa: A Cluster Randomised Trials. *Lancet*, 368, 1973-1983.
- Raftery, J. (1999). Methodological Limitations of Cost-effectiveness Analysis in Health Care: Implications for Decision Making and Service Provision. *Journal of Evaluation in Clinical Practice*, 594, 361-366.
- Raniga, T. & Simpson, B. (2011). Poverty, HIV/AIDS and the Old Age Pension in Bhambayi, KwaZulu-Natal, South Africa. *Development Southern Africa*, 28 (1), 75-88.
- Raogupta, G., Parkhurst, J. O., Ogden, J. A., Aggleton, P. & Mahal, A. (2008). A Structural Approach to HIV Prevention. *Lancet*, 372, 764-765.
- Rehle, M. & Shisana, O. (2003). Epidemiological and Demographic HIV/AIDS Projections: South Africa. *African Journal of AIDS Research*, 2(1), 1-8.
- Rehle, T., Shisana, O., Pilla, V., Zuma, K., Puren, A. & Parker, W. (2007). National HIV Incidence Measures –New Insights into the South African Epidemic. *South African Medical Journal*, 97, 194-199.
- Roger, L. (2009). IAS applauds South African Government for Commitment to Dramatically Scale-up HIV Treatment and Urges all Countries to Meet their HIV/AIDS Treatment. International AIDS Society (IAS), news release, July, 31.
- Rosen, S & Long, L. (2006): How Much Does It Cost to Provide Antiretroviral Therapy for HIV/AIDS in Africa. Health and Development. *Discussion Paper No. 9*. Centre for international health and development, Boston University.
- Rosen, S., Long, L; Sanne, I. (2008). The Outcomes and Outpatients Costs of Different Models of Antiretroviral Delivery in South Africa. *Tropical Medicine & International Health*, 13, 1005-1015.
- Rosenstock, I M. (1974). Historical Origins of the Health Belief Model. *Health Educ Monograph*, 2, 238-335.
- Ross, A, Camacho-Gonzales, A., Henderson, S., Abanyie, F., and R Chakraborty, R. (2010). The HIV-infected adolescent. *Current Infectious Disease Report* 12 (2010): 63-70.

- Sanders, G. D., Bayoumi, A. M. & Sundaram, V. (2005). Cost-effectiveness of Screening for HIV in the Era of Highly Active Antiretroviral Therapy. *New England Journal of Medicine*, 352(6), 370-584.
- Sax, P.E., Islam, R., Walensky, R., Losina, E., Weinstein, M.C., Goldie, S.J. Sadownik, S.N. & Freedberg, K.A. (2005). Should Resistance Testing be performed for Treatment Naïve HIV Infected Patients? A Cost-effectiveness Analysis. *Clinical & Infectious Diseases*, 41(1), 1316-1323.
- Schneider, H. & Stein, J. (2001). Implementing AIDS Policy in Post-Apartheid South Africa. *Social Science and Medicine*, 52, 723-731.
- Schneider, H., Hlope, H. & VanRensburg, D. (2008). Community Health Workers and the Response to HIV/AIDS in South Africa: Tensions and Prospects. *Health Policy and Planning*, 23, 179-187.
- Shaffer N, Chuachoowong R., Mock P.A., Bhadrakom, C., Siriwasin, W., Young, N.L., Chotpitayasunondh, T., Chearskul, S., Roongpisuthipong, A., Chinayon, P., Karon, J., Mastro, T.D, Simonds R.J (1999). Short-course Zidovudine for Perinatal HIV-1 Transmission in Bangkok, Thailand: A Randomised Controlled Trial. *Lancet* 353:773-780
- Shisana, O. & Simbayi, L.C. (2002). *Nelson Mandela/HSRC Study of HIV/AIDS : South African National HIV Prevalence, Behavioural Risks and Mass Media: Household Survey 2002*: Cape Town. HSRC.
- Sibeko, S. & Moodley, J. (2006). Health Care Attendance Patterns by Pregnant Women in Durban, South Africa. *South African Family Practice*, 48 (10), 17-24.
- Sinanovic, E., Floyd, K., Dudley, L., Azevedo, N., Grant, R., & Maher, D. (2003). Cost-effectiveness of Community-based Care for Tuberculosis in Cape Town, South Africa. *International Journal of Tuberculosis and Lung Diseases*, 7(9), 556-562.
- Skordis, J. & Natrass, N. (2002). Paying to Waste Lives: The Affordability of Reducing Mother-to-Child Transmission of HIV in South Africa. *Journal of Health Economics*, 21, 405-421.
- Snelling, D., Rasugu, D.D.W., Hong, S., Georgiades, K., Racine, Y. & Boyle, M.H. (2007). HIV/AIDS Knowledge, Women's Education, Epidemic Severity and Protective Sexual Behaviour in Low- and Middle-income Countries. *Journal of Biosocial Science*, 39 (3), 421-442.
- Soderlund, N., Zwi, K. & Kinghorn, A. (1999). Prevention of Vertical Transmission of HIV: Analysis of Cost-effectiveness of Options Available in South Africa. *Biomedical Journal*, 318, 1650-1656.
- Soderlund, N., Lavis, J. & Broomberg, J. (1993). The Cost of HIV Prevention Strategies in Developing Countries. *Bulletin of the World Health Organisation*, 75 (1), 595-604.

- Sonnenberg, F. & Beck, J. R. (1993). Markov Models in Medical Decision Making: A Practical Guide. *Medical Decision Making*, 13, 322-339.
- Soorapath, S., Sansom, S., Bulterys, M., Besser, M., Theron, G. & Fowler, M.G. (2006). Cost-effectiveness of HIV Rescreening during Late Pregnancy to Prevent Mother-to-Child Transmission in South Africa and Other Resources Limited Setting. *Journal of Acquired Immune Deficiency Syndrome*, 42 (2), 213-221.
- South African National AIDS Council (SANAC). (2010 a). The National HIV Counselling and testing Campaign strategies. SANAC Secretariat
- South African National AIDS Council (SANAC) (2010 b). The National HIV counselling and Testing Campaign. February.
- South African National AIDS Council (SANAC). (2012). National Strategic Plan on HIV, STI and TB 2012-2016. Accessed at <http://www.sanac.org.za>, on 12/09/2012
- Spanish Commission for Reducing Health Inequalities. (2007). Socio-economic Determinants of Health. Accessed at <http://www.instituteofhealthequity.org/projects/spanish-commission-to-reduce-inequalities-in-health>, on 10/03/2012 check
- Stanley, N. & Duplessis, J.A(2005). The Cost of a Rapid Test VCT Clinic in South Africa. *South African Medical Journal*, 95(12).968-971.
- Sterling, M., Rees , H., Kasede, S. & Harkins, C. (2008). Introduction: Addressing the Vulnerability of Young Women and Girls to Stop HIV Epidemic in Southern Africa. *AIDS*, 22 (Supl 2), S1-S3.
- Stewart, S. (2010). South Africa Launches Massive HIV Prevention and Treatment Campaign. *UNAIDS Press*: 25 April.
- Statistics South Africa. (2010). *Mid-year Population Estimates*, Accessed at <http://www.statssa.gov.za/Publications/P0302/P03022013.pdf>, on 14/05/2013
- Statistics South Africa (2011). Mid-year population estimates 2011. Statistics South Africa, Pretoria.
- Statistics South Africa. (2013). *Mid-year population estimates*. Pretoria. Accessed at <http://www.statssa.gov.za/Publications/P0302/P03022013.pdf>, on 14/05/2013
- Stover, J (2009). *AIM: A Computer Programme for Making HIV/AIDS Projections and Examining the Demographic and Social Impacts of AIDS*. Wahsington DC. Future Group International. Health Policy Initiative, Task Order I.

- Sweat, M., Gregorich, S., Sangiwa, G., Furlonge, C., Balmer, D., Kamenga, C., Grinstead, O & Coates, T. (2000). Cost-effectiveness of Voluntary HIV1-Counselling and Testing in Reducing Sexual Transmission of HIV1 in Kenya and Tanzania. *Lancet*, 356, 113-121.
- Sweeney, S., Obure, C.D., Maier, C.B., Greener, R., Dehne, C.& Vassall, A. (2012). Cost and Efficiency of Integrating HIV/AIDS Services with other Health Services: A Systematic Review of the Evidence and Experience. *Sexually Transmitted Infections*, 88, 85-99.
- Tindyebwa, D., Kayita, J., Musoke, P., Brian, E.& Nduati, R., (2006). *Handbook of Paediatric AIDS in Africa*. Nairobi. African Network on the Care of Children Affected by AIDS.
- Tiruneh, G. (2009). Determinants of HIV/AIDS Prevalence in Africa: Do Cultural Variations Matter? *Midsouth Political Science Review*, 10, 103-123.
- Tladi, L.S. (2006). Poverty and HIV/AIDS in South Africa: An Empirical Contribution. *Journal of Social Aspects of HIV/AIDS*, 3 (1), 369-381.
- Tufte, T. (2002). Edutainment in the HIV/AIDS Prevention: Building on the Soul City Experience in South Africa. In Servaes, J. (ed.), *Approach to Development Communication*, Paris: UNESCO.
- Tshabalala, M.E. (2012). Utilisation of Antinetal Care (ANC) and Prevention of Mother-to-child Transmission of HIV (PMTCT) Services in East Ekhluleni Sub-District, Gauteng province, South Africa. Thesis. UNISA.
- UNAIDS. (2009). Spectrum 2009, Estimates and Projections of National HIV/AIDS epidemic. [Power Point presentation.] Geneva:UNAIDS.
- UNAIDS. (2011 a). *Global Report:UNAIDS Report on the Global AIDS Epidemic 2011*. Geneva, UNAIDS.
- UNAIDS. (2011 b). *UNAIDS World AIDS Day Report*. Geneva. UNAIDS.
- UNAIDS. (2012). *UNAIDS World AIDS Day Report*. Geneva. UNAIDS.
- United Nations' Population Division.(2011). Population statistics
- USAID. (2005). *A Study of the Burden of HIV and AIDS and Impact of HIV and AIDS on the Health Sector in Swaziland*. Health and Development Africa. Commissioned by the Ministry of Health and Social Welfare. USAID
- Uys, L & Heshner, M. (2009). The Cost of Home-based Care for People with HIV/AIDS in South Africa. *South African Medical Journal*, 92 (8), 624-628.

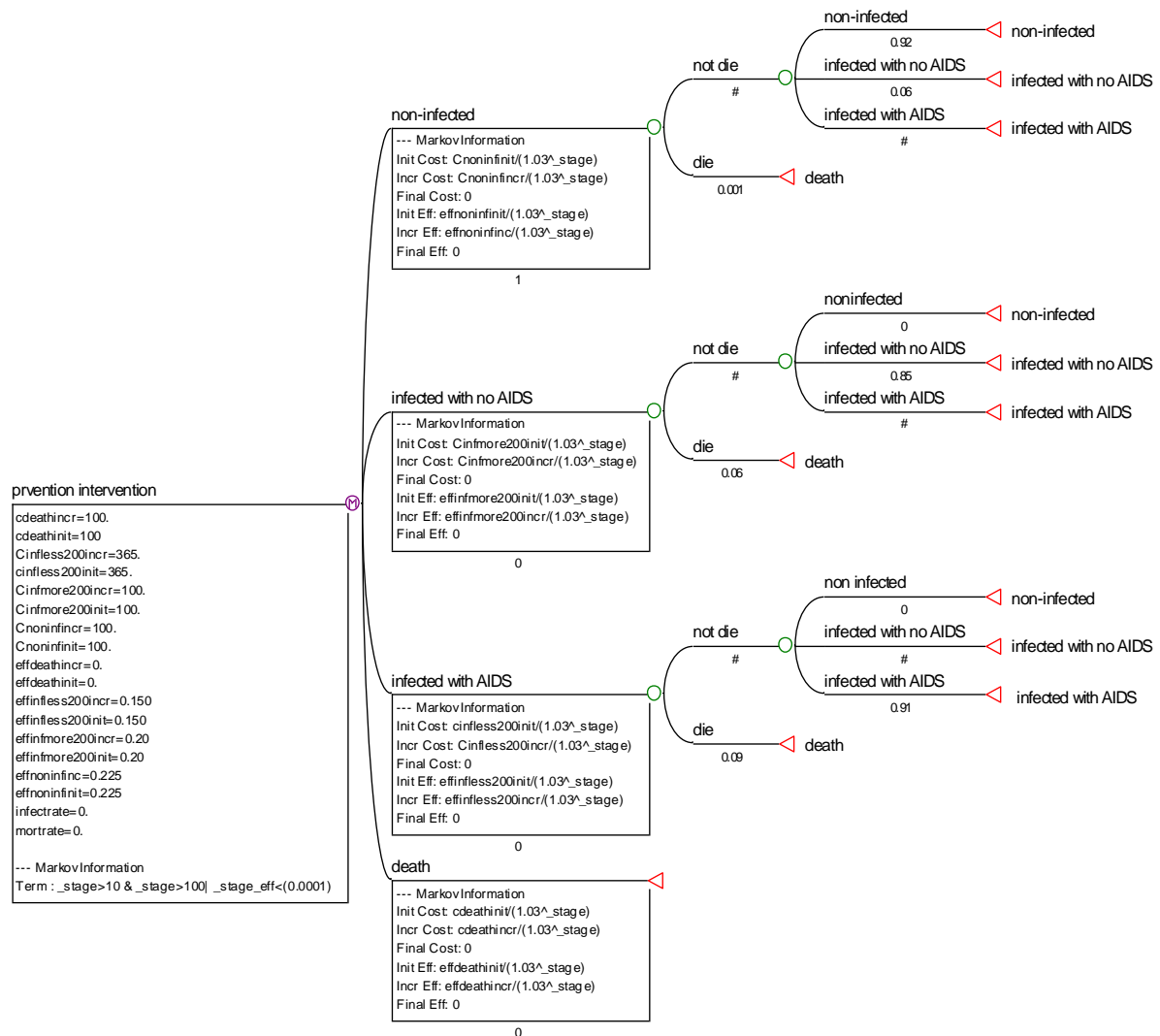
- Valentine, N. & Solar, O. (2011). The Conceptual Framework for Social Determinants of Health. Which Theory is the Basis for Tool for Health Impact Assessment. Power Point Presentation. Department of Ethics, Equity, Trade and Human Rights / WHO. Accessed at si.easp.es/../.VandePierre, on 06/06/2012.
- VanRie, A., Beyers, N., Gie, P.R., Kuneke, M., Zietsman, L. & Donald, P.R. (1999). Childhood Tuberculosis in a Urban Population in South Africa. *Archives of Child Health*, 80, 433-437.
- Vass, J. (2007). A Review of Labour Markets in South Africa: The Impact of HIV/AIDS on the Labour Markets HSRC/SIDA . Employment Growth & Development Initiative. Pretoria. HSRC
- Verguet, S. & Walsh, J.A. (2010). Vaginal Microbicides Save Money: A Model of Cost-effectiveness in South Africa and the USA. *Sexually Transmitted Infections*, 86 (3), 212-216.
- Vickerman, P., Terris-Prestholt, F., Delany, S., Kumaranayake, L., Rees, H. & Watts, C. (2006 a). Are Targetted HIV Prevention Activities Still Cost-effective in High Prevalence Settings? Results From an STI Treatment Interventions For Sex Workers in HillBrow, South Africa. *Sexually Transmittable Diseases*, 33 (10), S122-S132.[Vickerman *et al.*, 2006 a]
- Vickerman, P; Watts, C; Delany, Alany, M., Rees, H. & Heise, L. (2006 b). The Importance of Context: Model Projections on How Microbicide Impact Could Be Affected by the Underlying Epidemiological and Behavioural Situation in Two African Settings. *Sexually Transmitted Diseases*, 33, 397-495. [Vickerman *et al.*, 2006 b]
- Walensky, R. P., Wood, R., Weinstein, M. C., Martinson, M. A., Losina, E., Fofana, M. O. & CEPAC International Investigators. (2008). Scaling up Antiretroviral Therapy in South Africa: The Impact of Speed on Survival. *Journal of Infectious Diseases*, 197, 1324-1332.
- Walensky, R.P., Wood, R., Fofana, M.O., Martinson, N.A, Losina, E., April .M.D., Basett, I.V., Morris, B.L., Freedberg, K.A. & Partiel, A.D. (2011). The Clinical Impact and Cost-effectiveness of Routine Voluntary HIV Screening in South Africa. *Journal of Acquired Immune Deficiency Syndrome*, 56, 26-35.
- Walker, D. (2003). Cost and Cost-effectiveness of HIV/AIDS Prevention Strategies in Developing Countries: Is There Evidence Base? *Health Policy and Planning*, 18 (1), 4-17.
- Wallrauch, C., Heller, R., Lessells, R., Kakana, M., Barghaussen, T. & Newell, M.L (2010). High Uptake of HIV Testing for Tuberculosis Patients in an Integrated Primary Health Care HIV/TB Programme in Rural KwaZulu-Natal. *South African Medical Journal*, 100 (3), 146-147.

- Wegbreit, J., Bertozzi, S., DeMaria, L.M., & Padian, N.S. (2006). Effectiveness of HIV Prevention Strategies in Resource-poor Countries: Tailoring the Intervention to the Context. *AIDS* 20, 1217-1235.
- Weiss, R. A. (2008). Special Anniversary Review: Twenty Five Years of Human Immunodeficiency Virus Research: Success and Challenges. *Clinical Experimental Immunology*, 152, 201-210.
- White, R.G., Orroth, K.K., Glynn, J.R., Freeman, E.E., Bakker, R., Habbema, J.D, Terris-Prestholt, F., Kumaranayake, L., Buve, A. & Hayes, R.J. (2008). Treating Curable Sexually Transmitted Infections to Prevent HIV in Africa: Still an Effective Control Strategy? *Journal of Acquired Immunodeficiency Syndrome*, 47 (3), 346-353.
- Whiteside, A. & Smith, J. (2009). Exceptional Epidemics: AIDS still Deserves a Global Response. *Globalisation and Health* 5: 15.
- Wilkinson, D., Floyd, K. & F, G. C. (1998). Antiretroviral Drugs as a Public Health Intervention for Pregnant HIV-infected Women in Rural South Africa : An Issue of Cost-effectiveness and Capacity. *AIDS*, 12, 1675-1682.
- Wilkinson, D., Floyd, K. & Gilks, F. C. (2000). National and Provincial Estimated Costs and Cost-effectiveness of a Programme to Reduce Mother-to-Child HIV Transmission in South Africa. *South African Medical Journal*, 90 (8), 794-798.
- Williams, B.G., Taljaard, D., Campbell, C.M., Gouws, E., Ndhlovu, L., VanDam, J. & Auvert, B. (2003). Changing Patterns of Knowledge, Reported Behaviors and Sexually Transmitted Infections in a South African Gold Mining Community. *AIDS*, 17 (14), 2099-2107.
- World Health Organisation (WHO) (2002). *Report of the Commission on Macroeconomics and Health*. Geneva. World Health Organisation
- World Health Organisation (WHO). (2003). *Making Choices in Health: WHO Guide to Cost-effectiveness Analysis*, Geneva. World Health organisation
- World Health Organization(WHO), (2007). *Preferred Antiretroviral Medicines for Treating and Preventing HIV Infection in Younger Children*. Report of the WHO Paediatric Antiretroviral Working Group
- Wood, E., Braitstein, P., Montaner, J.S., Schechter, M. & Tyndall, M. (2000). Extent to which Low-level use of Antiretroviral Treatment Could Curb the AIDS Epidemic in Sub-Saharan Africa. *Lancet*, 355, 2095-2100.
- Yeap, A.D., Hamilton, R., Charalambous, S., Dwadwa, T., Churchyard, G.J., Geisser, P.W. & Grant, AD. (2010). Factors Influencing Uptake of HIV Care and Treatment among Children in South Africa-A Qualitative Study of Caregivers and Clinic Staff. *AIDS*, 229 (9), 1101-107.

- Young, S.D., Hlavka, Z., Modiba, P., Gray, G., FCPaeds(SA) & VanRooyen, H. (2010). HIV-related Stigma, Social Norms, and HIV Testing in Soweto and Vulindlela, South Africa: National Institutes of Mental Health Project Accept(HPTN). *Journal of Acquired Immunodeficiency syndrome*, 55, 620-624
- Zanakis, S.H., Alvaez, C., & Li, V.(2007). Socio-economic Determinants of HIV Pandemic and nations Efficiencies. *European Journal of Operational Research*, 176:1811-1838.
- Zelinick, J.& O'Donnell, M. (2005). The Impact of HIV/AIDS Epidemic on Hospital Nurses in KwaZulu-Natal, South Africa: Nurses' Perspectives and Implications for Health Policy. *Journal of Public Health Policy*, 26, 163-185.
- Zwang, J., Garenne, M., Kahn, K., Collinson, M.& Tollman, S.M. (2007). Trends in Mortality from Pulmonary Tuberculosis and HIV/AIDS Co-infection in Rural South Africa (AginCourt). *Transaction of the Royal Society of Tropical Medicine and Hygiene*, 101(9), 893-898.
- Zwi, A. & Bachmayer, D. (1990). HIV and AIDS in South Africa: What is an Appropriate Public Health Response ? *Health Policy and Planning*, 5(4), 316-326.

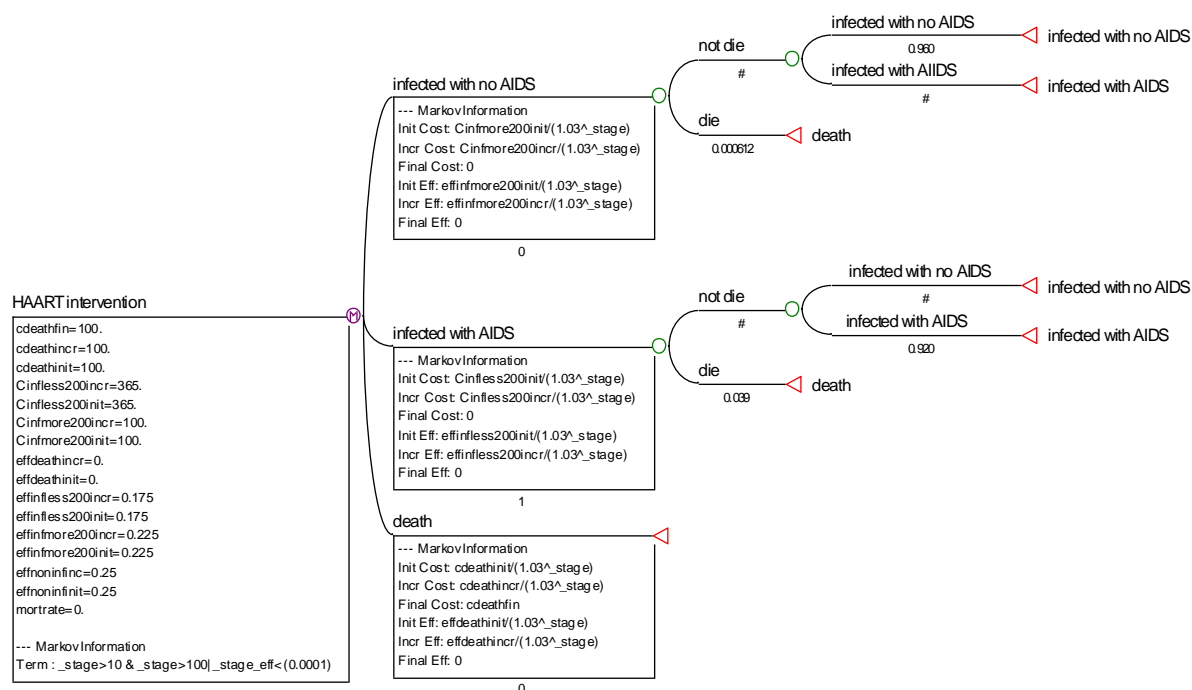
APPENDICES

Appendix 1: A typical Markov cycle tree structure for an HIV/AIDS prevention intervention in a given HIV prevalence context



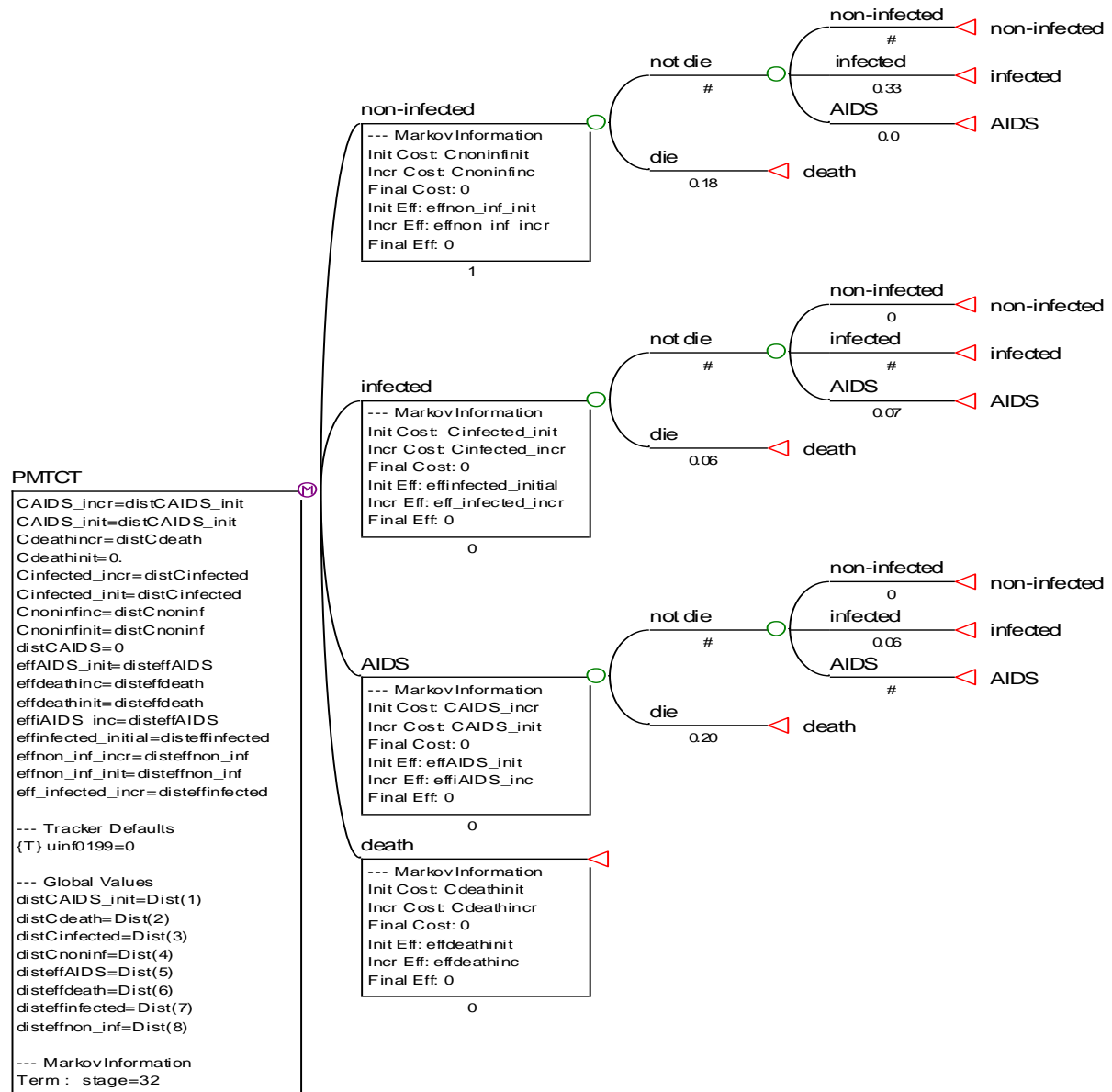
Note: data in this model structure changes with the type of intervention (VCT, STD, or PMTCT) and the type of context (an LPC or a HPC) but the structure of Markov model is the same

Appendix 2: A typical Markov cycle tree structure for a HAART intervention in a given HIV prevalence context

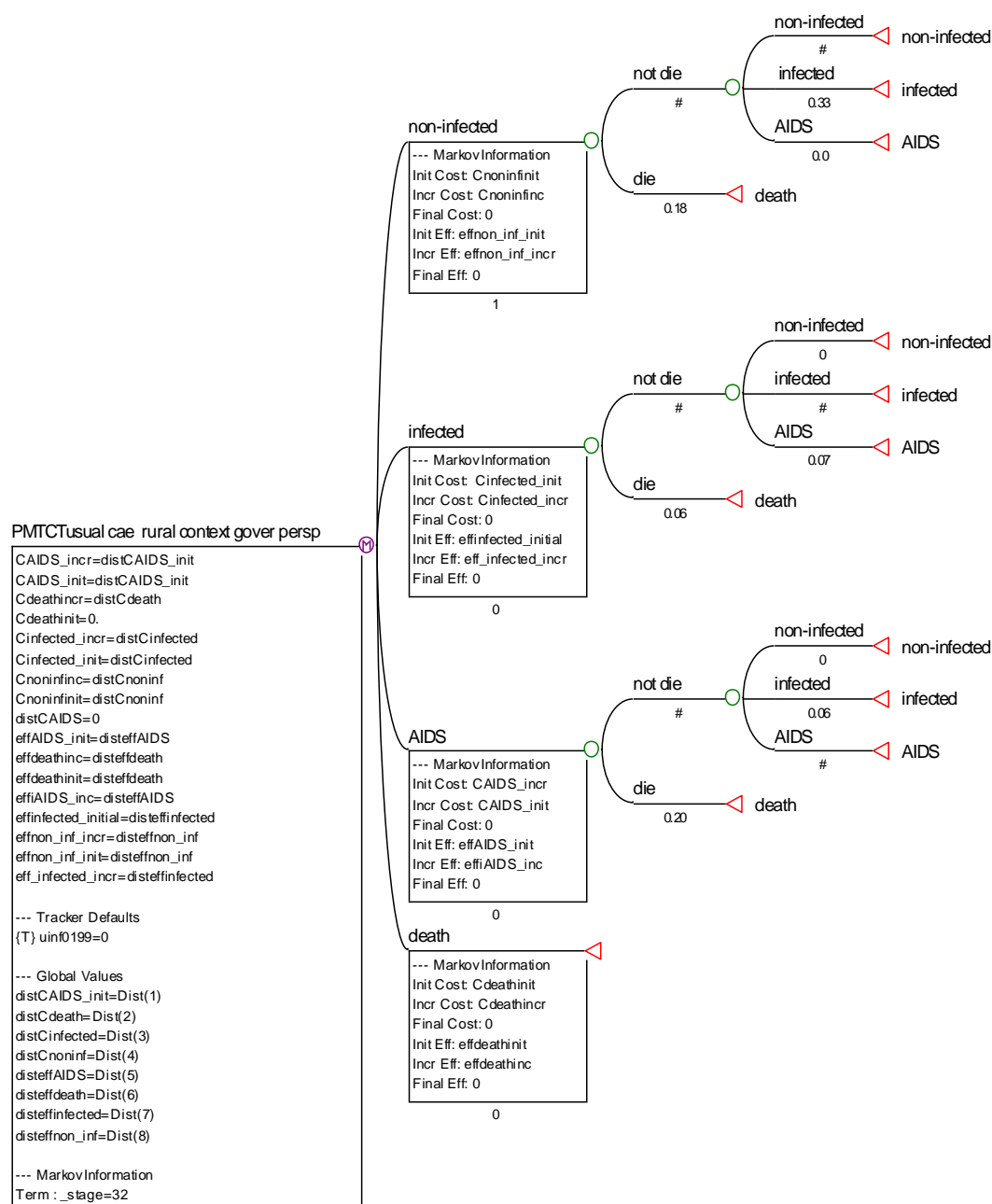


Note: data in this model structure changes with the type of intervention (VCT, STD, or PMTCT) and the type of context (an LPC or a HPC) but the structure of Markov model is the same

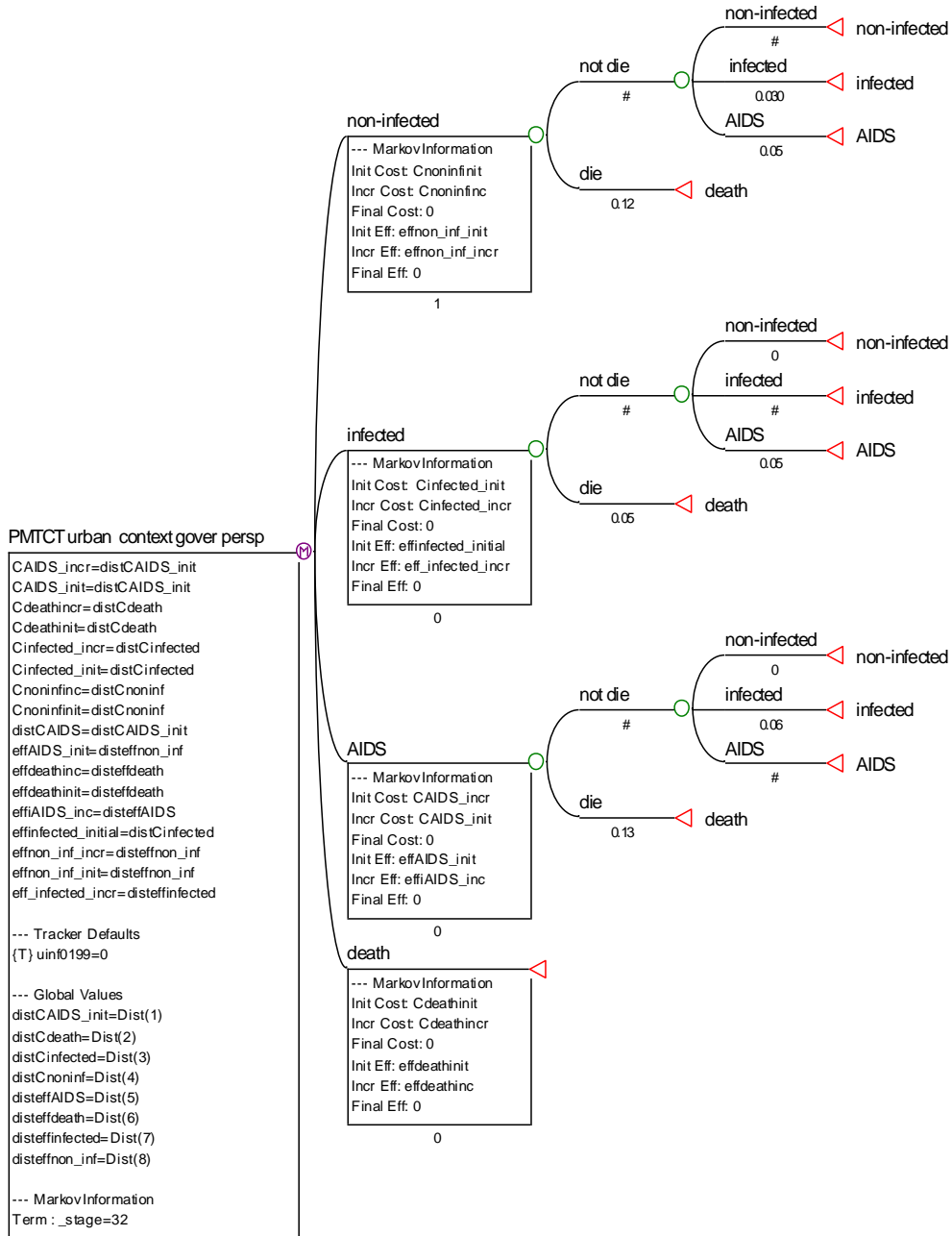
Appendix 3: A typical Markov cycle tree structure for PMTCT in a rural context (base-case analysis)



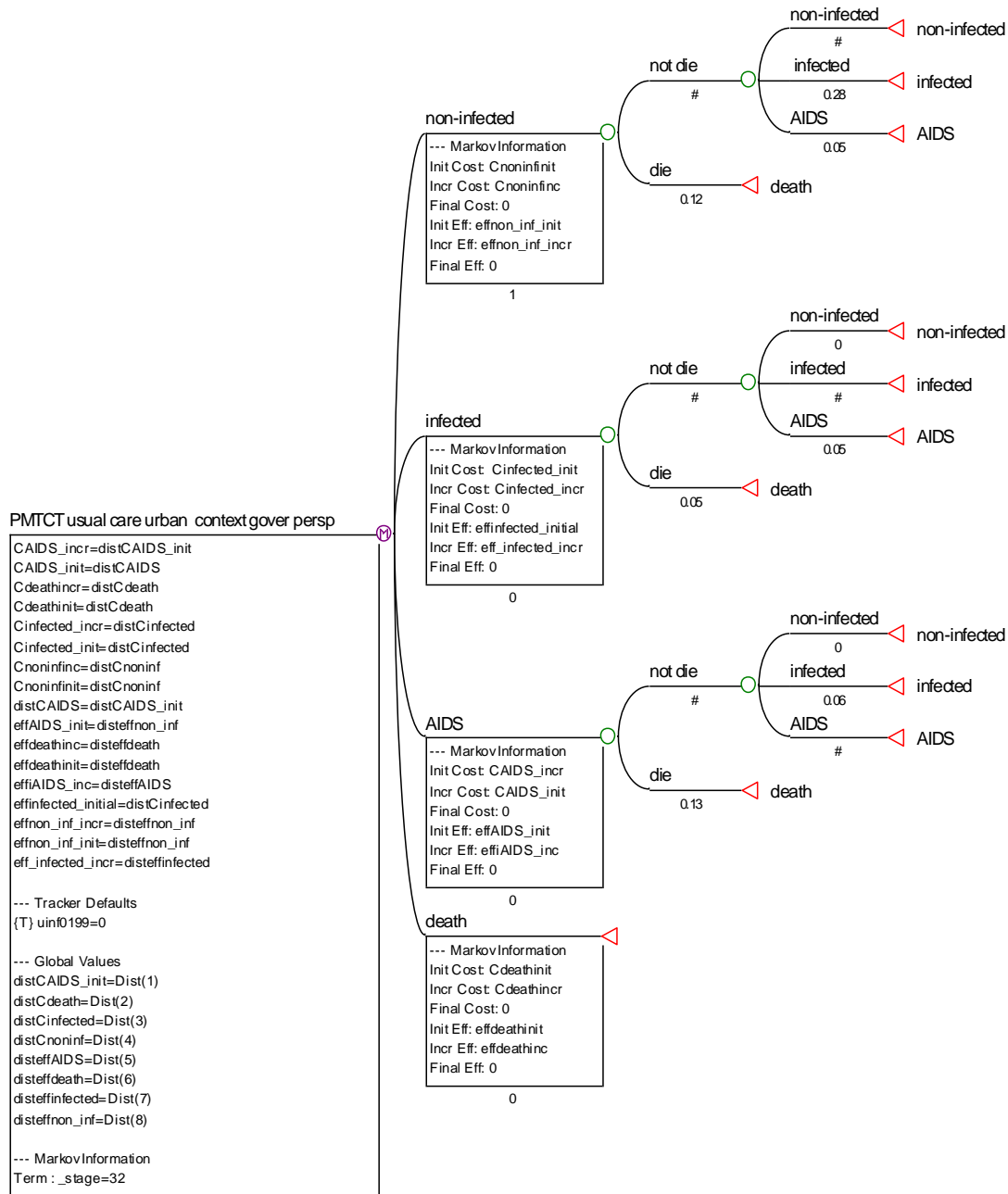
Appendix 4: A typical Markov cycle tree for USUAL CARE related to PMTCT in a rural context



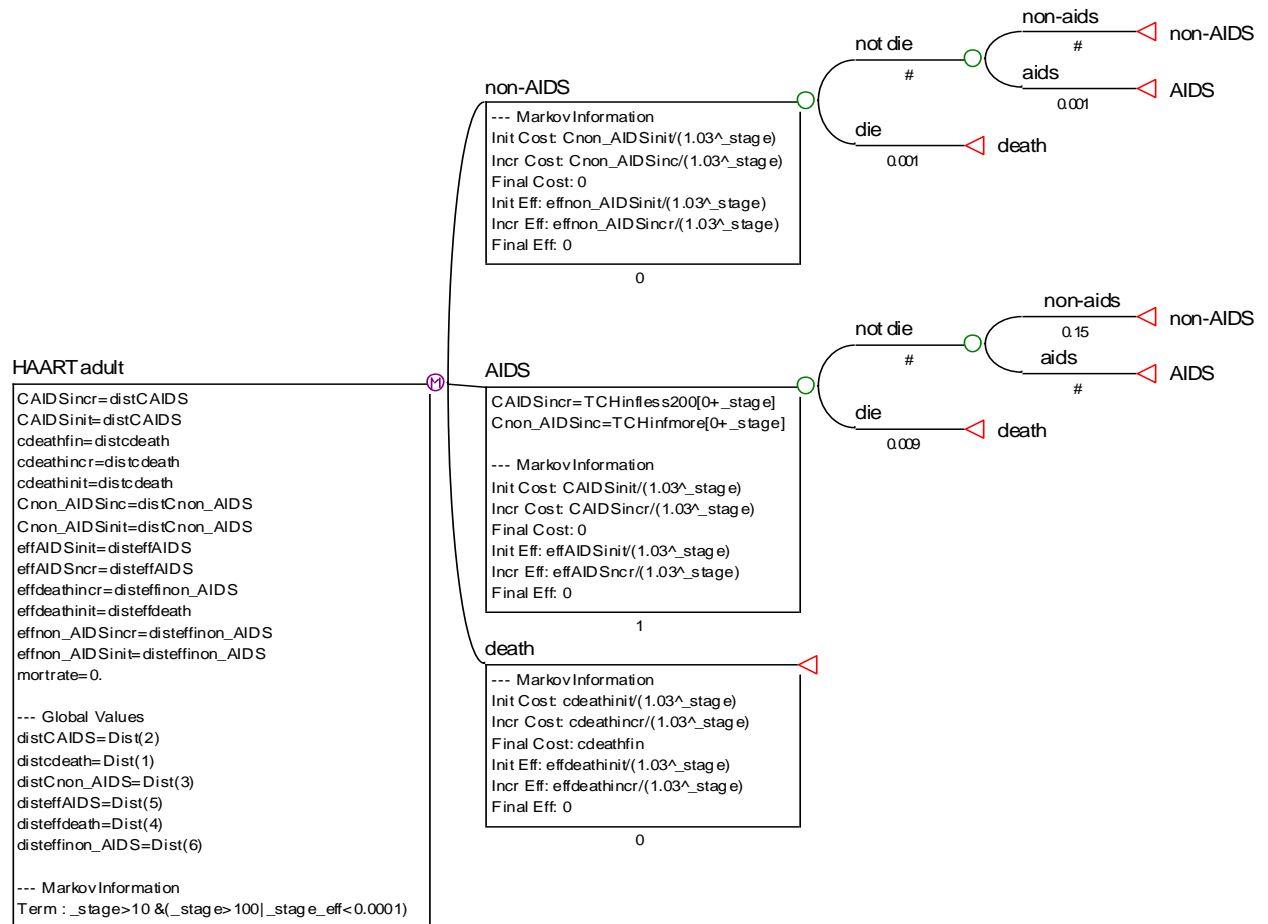
Appendix 5: A typical Markov cycle tree for PMTCT in an urban context



Appendix 6: A typical Markov cycle tree for USUAL CARE related to PMTCT in an urban context.

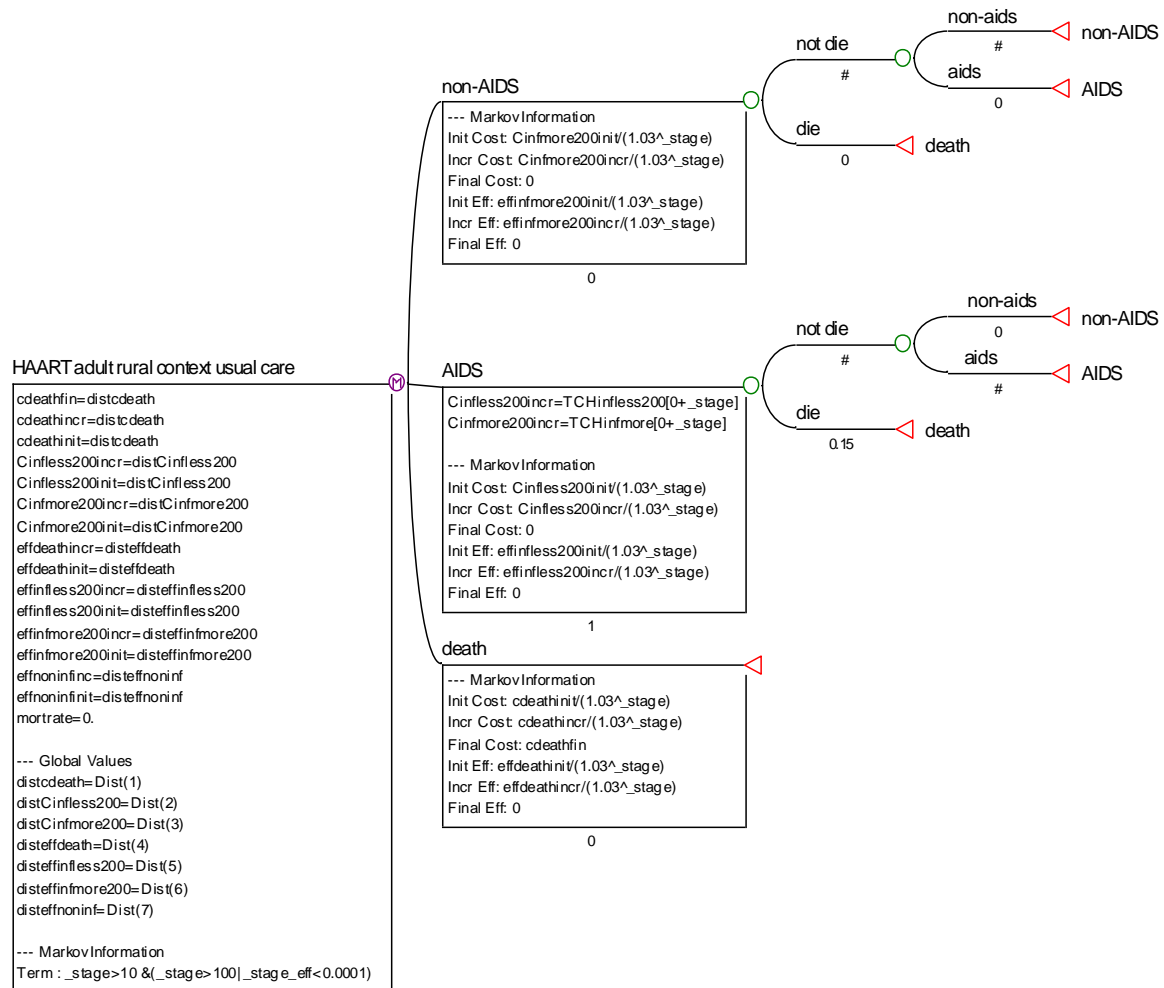


Appendix 7: A typical Markov cycle tree structure for a HAART FOR ADULTS in a rural context

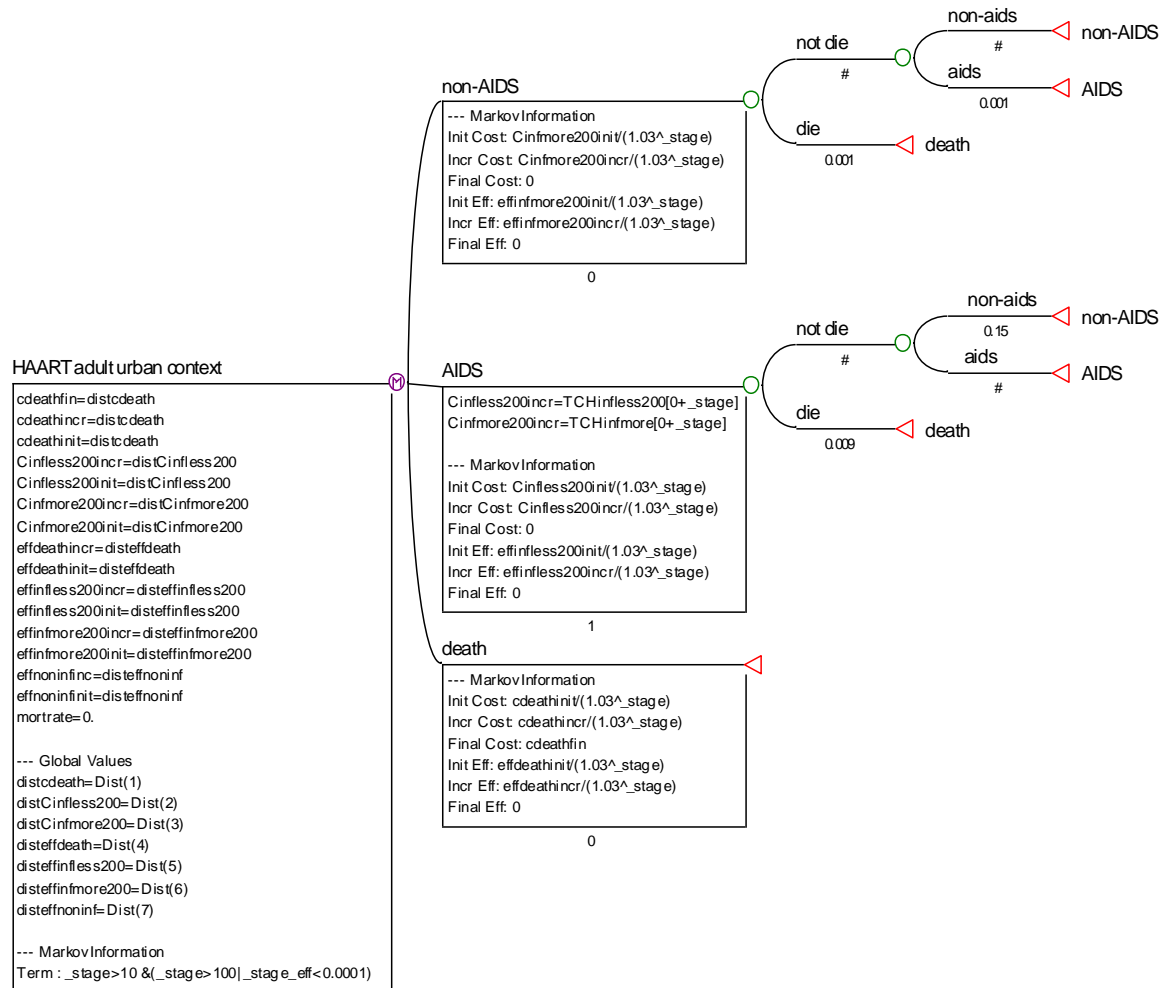


Note: data in this structure changes with type of population of patients (children or adults) and the type of intervention (HAART or USUAL CARE) and the type of context (rural or urban) but the structure of Markov model is the same.

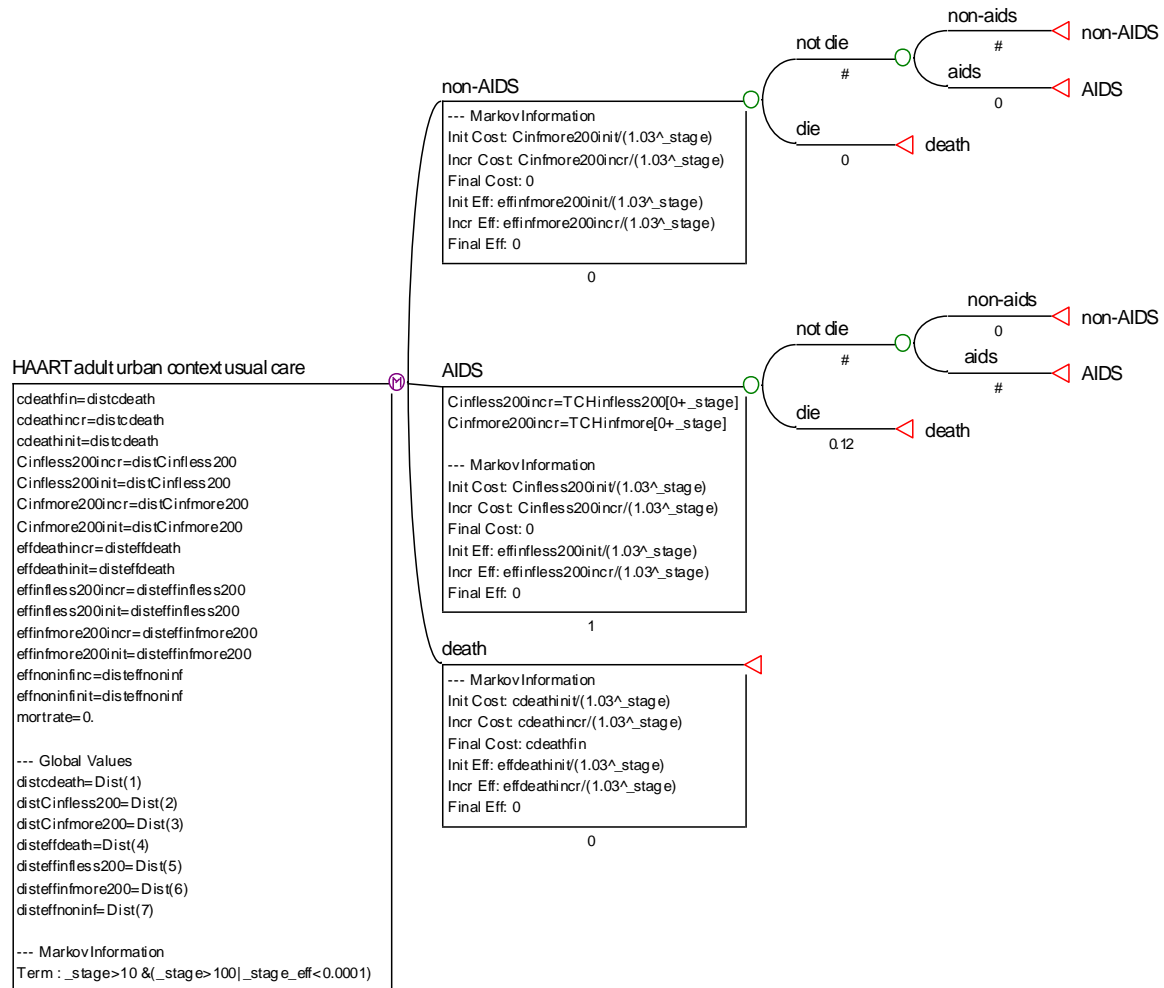
Appendix 8: A typical Markov cycle tree structure for USUAL CARE related to HAART FOR ADULTS in a rural context



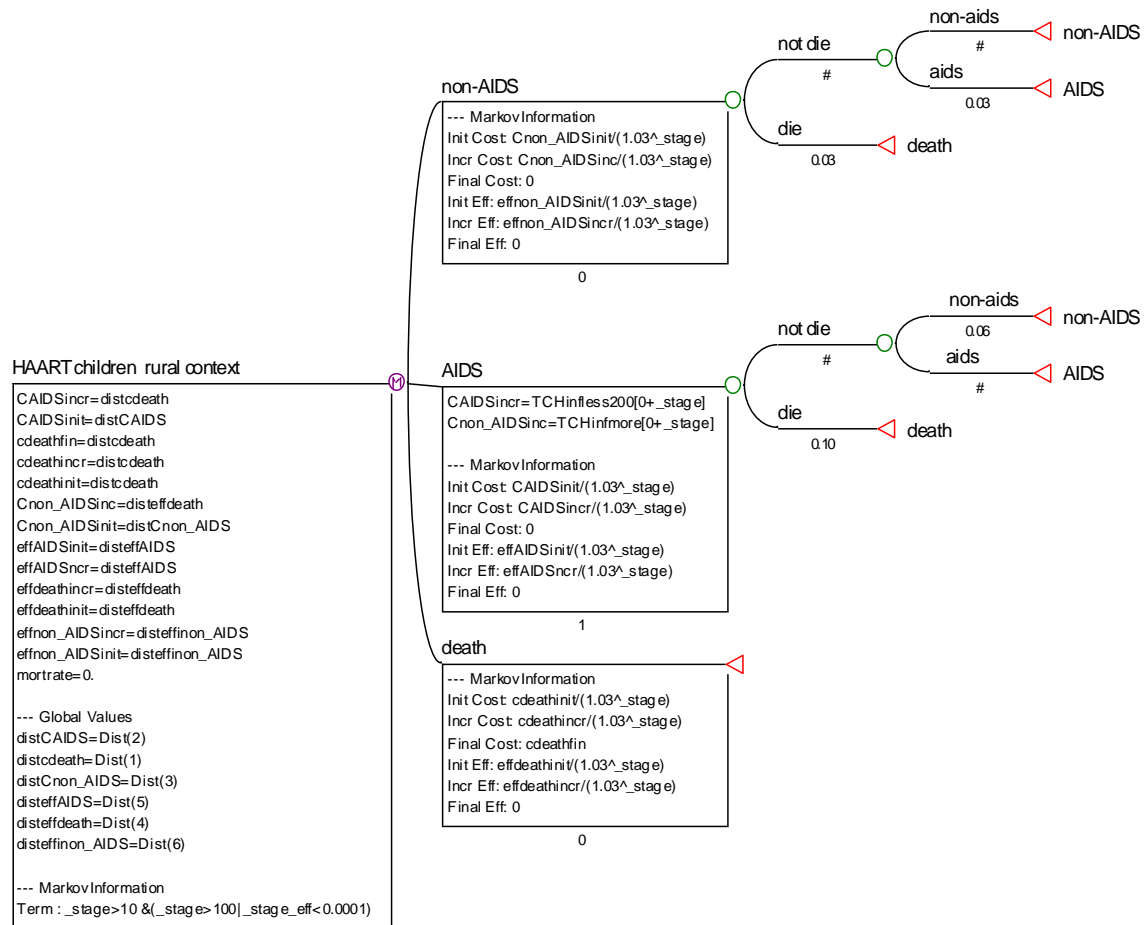
Appendix 9: A typical Markov cycle tree structure for a HAART FOR ADULTS in an urban context



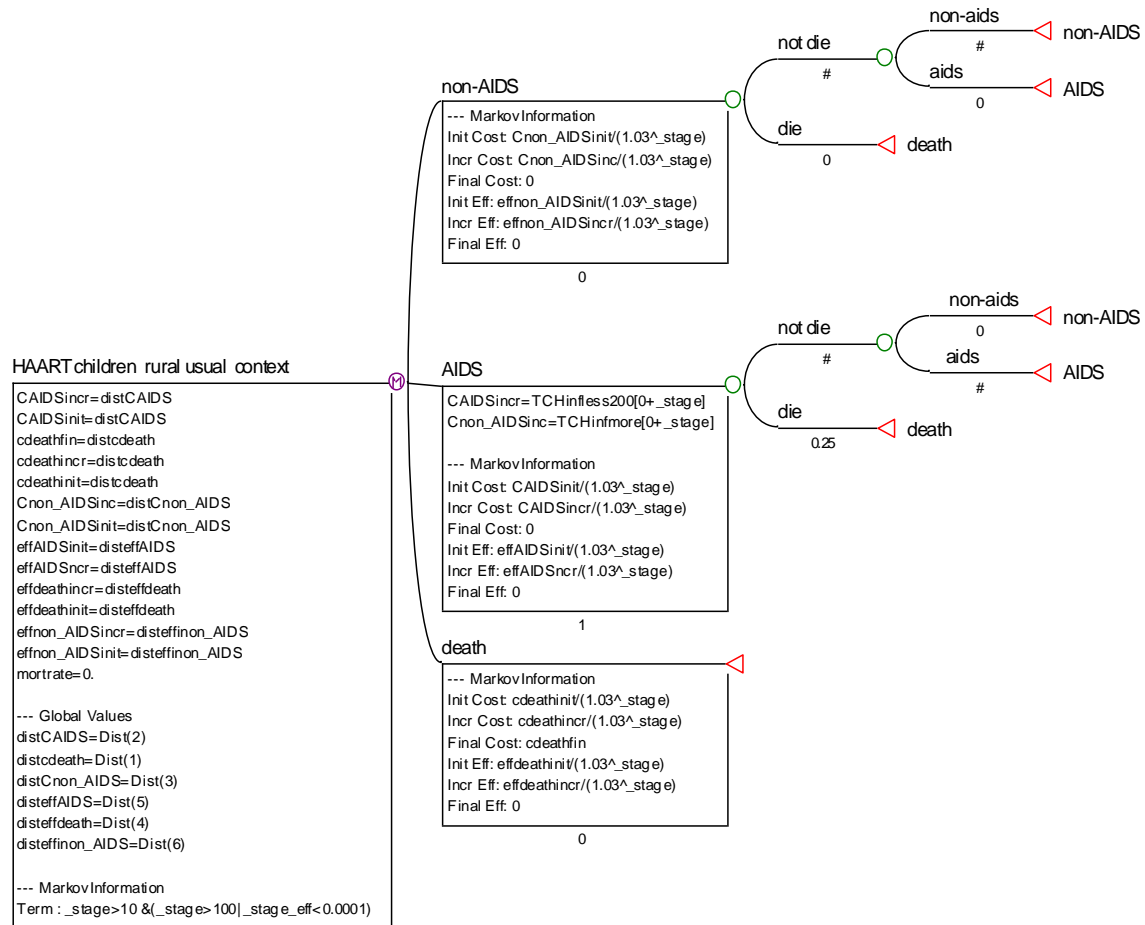
Appendix 10: A typical Markov cycle tree structure for USUAL CARE related to HAART FOR ADULTS in a urban context



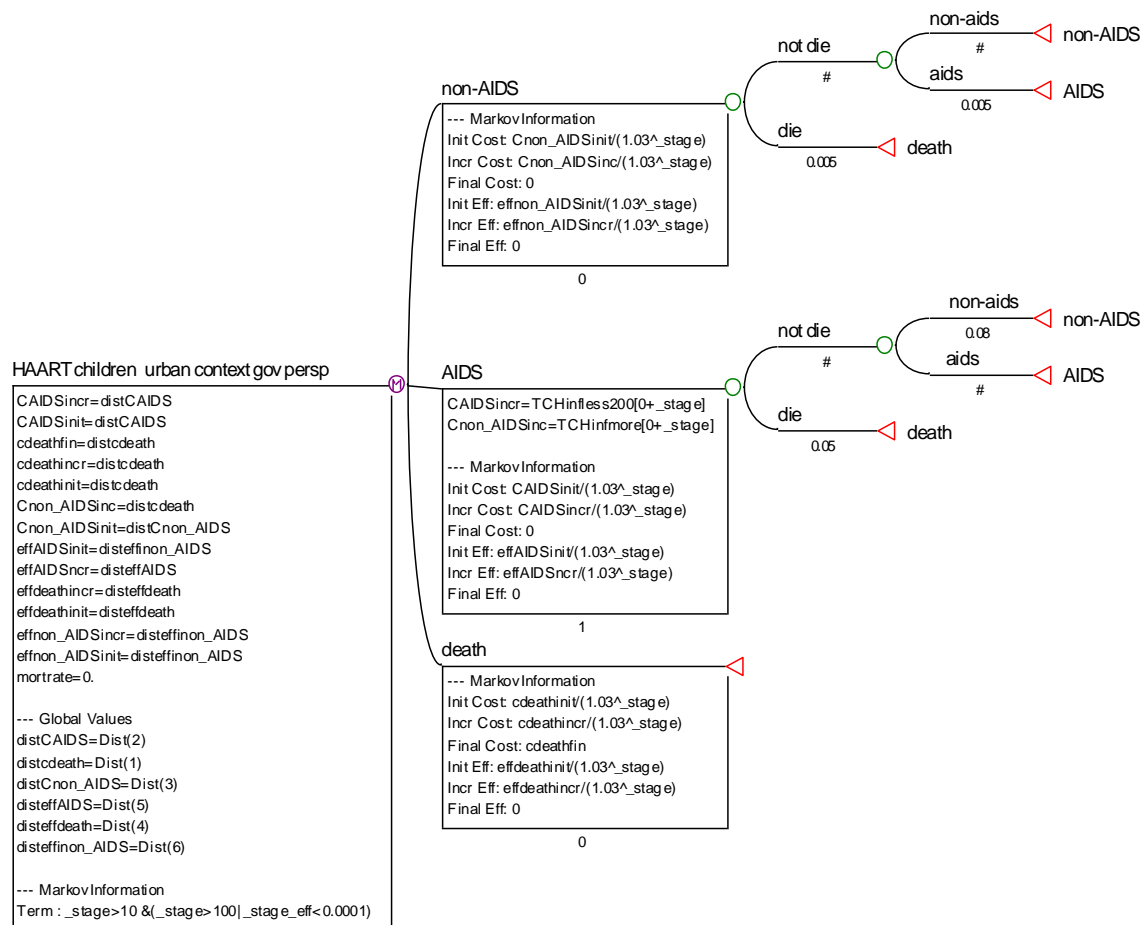
Appendix 11: A typical Markov cycle tree structure for a HAART FOR CHILDREN in a rural context



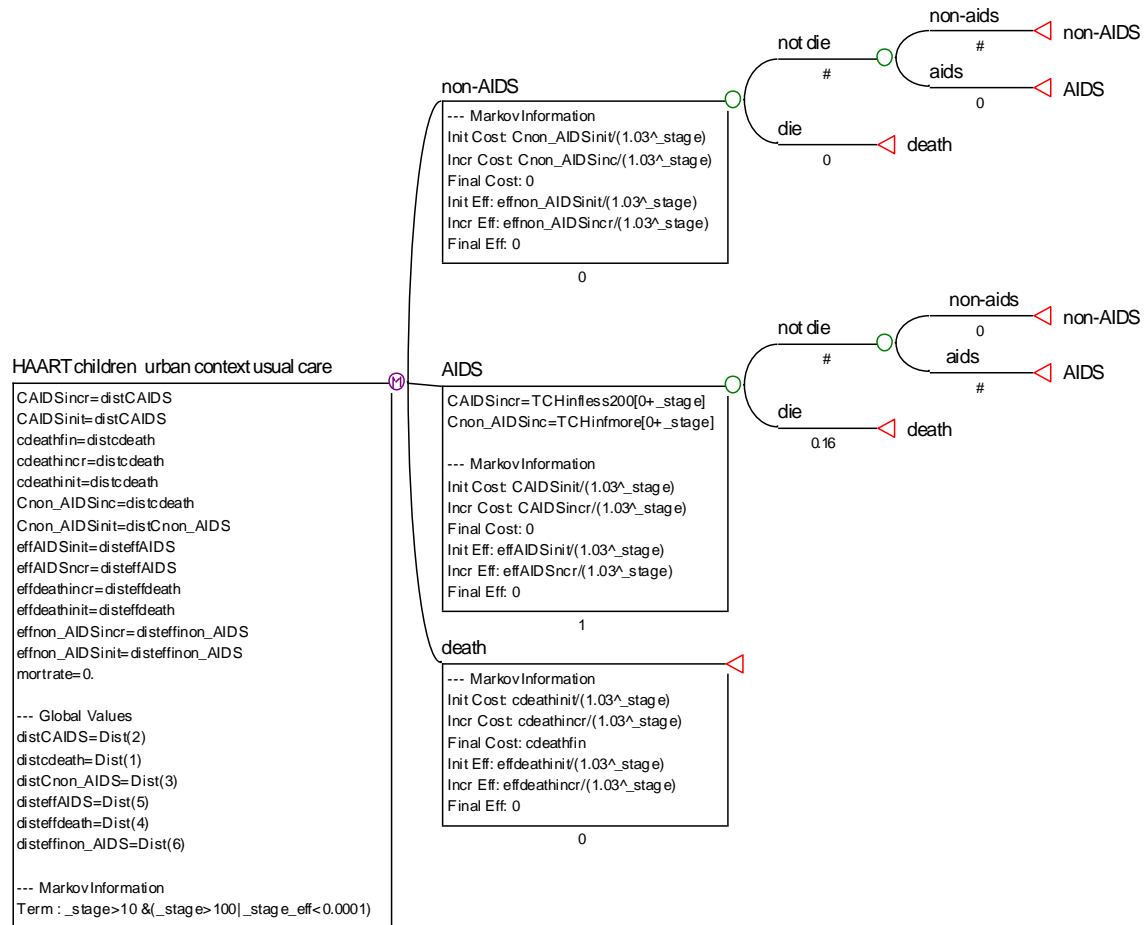
Appendix 12: A typical Markov cycle tree structure for USUAL CARE related to HAART FOR CHILDREN in an rural context



Appendix 13: A typical Markov cycle tree structure for a HAART FOR CHILDREN in an urban context



Appendix 14: A typical Markov cycle tree structure for USUAL CARE related to HAART FOR CHILDREN in a urban context

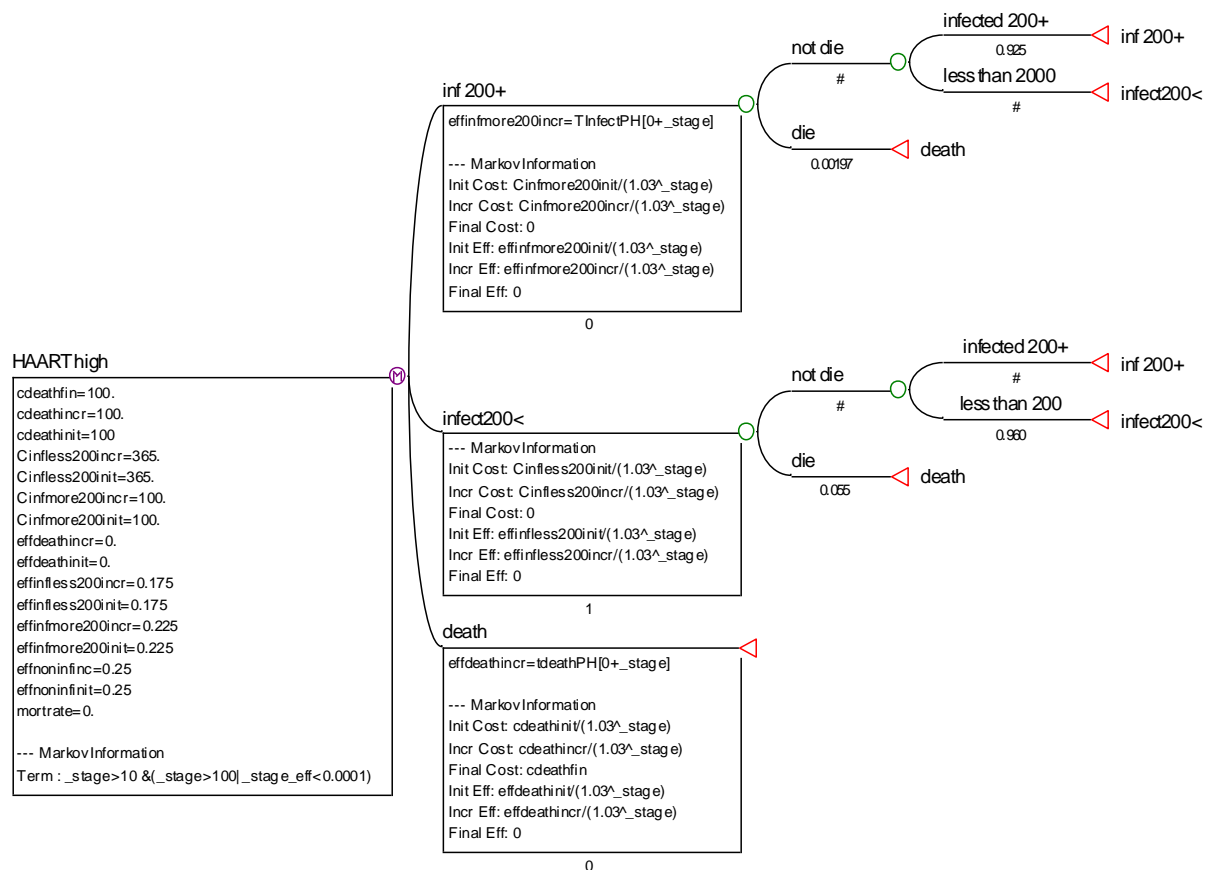


Appendix 15: explanation of how progression in subsequent states was pegged on ASSA 2008 AIDS model projections.

A simple way of evaluating the cost and effectiveness using Markov model is to assume the same transition probability matrix in all successive periods. The use of the same transition probability matrix assumes that the epidemic is constant. In the case of South Africa, the epidemic has not been constant since 2007. There has been decrease in new infections and mortality.

To take into account the decreasing HIV infections rates and HIV-related mortality rates, the study used the Table option in Markov. The Table option allows the application of decreasing infection rate and mortality rate on patients in an "infected" state and "death" state as per SPMS projections in each Markov period.

The Table option in TreeAge Pro consists of defining the variable's infection and mortality such that in the evaluation of the costs, the estimation is based on the patients in that state which in turn is determined by value in the Table reflecting the trend in the epidemic. The variables for which Tables were created in TreeAge pro were infected but not yet in need of treatment (effinmoreinc 200) and deaths (effdeathincr) as shown in the model structure for HAART in prevalence context below:



Since the cohort must be fully distributed in all HIV/AIDS states. Pegging transition probabilities to infections rates and deaths required adjustment of transition probabilities in the intermediates HIV/AIDS states.

To determine the proportion of infected and deaths in each Markov period in TreeAge Pro Table, annual estimates of average infection rate in each context, the LPC and the HPC, were obtained from the ASSA2008 AIDS model. ASSA2008 is an excel model developed by the Actaral Society of South Africa. These annual infection rates were then transformed into 3-month transition infection rates. The % decrease in the rate of infection or mortality from a three-month period to another was then applied to the previous period transition probability to determine the value to be recorded in the Table. The values in a treeAge pro Table for successive Markov periods will be picked up in the model evaluation of costs and effectiveness.

Appendix 16: explanation of how data were transferred from TreeAge Pro Software to excell for graphical and numerical analysis

Running Markov model in TreeAge pro allowed the transfer of data in excel for graphical nummemrical analysis. Below is an example of results of Markov models as they would appear in an excel spreadsheet for grahical analysis and numerical analysis.

Stage	Stage Cost	Stage Eff	Cumulative Cost	Cumulative Eff	P(inf 200+)	P(infect200<)	P(death)
0	95.58348	0.125	95.58348	0.125	0	1	0
1	84.88408	0.114284	180.4676	0.239284	0.0378	0.9072	0.055
2	75.67432	0.104739	256.1419	0.344024	0.069188	0.825841	0.10497
3	67.72495	0.096212	323.8668	0.440236	0.09509	0.754382	0.150528
4	60.84343	0.088573	384.7103	0.528809	0.116301	0.691493	0.192206
5	54.86792	0.081708	439.5782	0.610517	0.133504	0.636028	0.230468
6	49.66235	0.075522	489.2405	0.686039	0.14729	0.586998	0.265712
7	45.11219	0.069931	534.3527	0.75597	0.158164	0.543549	0.298287
8	41.12105	0.064865	575.4738	0.820835	0.166559	0.504947	0.328494
9	37.60765	0.060261	613.0814	0.881096	0.172851	0.470555	0.356594
10	34.50345	0.056066	647.5849	0.937162	0.177359	0.439826	0.382815
11	31.75059	0.052267	679.3355	0.989429	0.180359	0.412286	0.407355
12	29.30013	0.04879	708.6356	1.038219	0.182088	0.387526	0.430386
13	27.11069	0.0456	735.7463	1.083819	0.182748	0.365193	0.452059
14	25.14717	0.042666	760.8934	1.126485	0.182513	0.344982	0.472504
15	23.37981	0.039963	784.2733	1.166448	0.181533	0.32663	0.491838
16	21.78329	0.037465	806.0565	1.203913	0.179933	0.309906	0.51016
17	20.33606	0.035153	826.3926	1.239066	0.177825	0.294616	0.527559
18	19.01974	0.03301	845.4123	1.272076	0.175301	0.280586	0.544114
19	17.81861	0.031019	863.2309	1.303096	0.17244	0.267669	0.559891
20	16.71921	0.029167	879.9502	1.332263	0.16931	0.255737	0.574953
21	15.70996	0.027479	895.6601	1.359742	0.16597	0.244678	0.589352
22	14.78092	0.025904	910.441	1.385646	0.162469	0.234395	0.603136
23	13.92348	0.024431	924.3645	1.410077	0.158848	0.224804	0.616348
24	13.13019	0.023054	937.4947	1.433131	0.155142	0.215833	0.629025
25	12.39461	0.021763	949.8893	1.454894	0.151383	0.207416	0.641201
26	11.71108	0.020553	961.6004	1.475447	0.147593	0.199499	0.652908
27	11.0747	0.019417	972.6751	1.494864	0.143796	0.192033	0.664171
28	10.48115	0.01835	983.1563	1.513214	0.140008	0.184976	0.675016
29	9.926618	0.017346	993.0829	1.53056	0.136244	0.17829	0.685465
30	9.40776	0.016402	1002.491	1.546961	0.132517	0.171943	0.69554
31	8.9216	0.015512	1011.412	1.562474	0.128836	0.165906	0.705258
32	8.465493	0.014674	1019.878	1.577148	0.12521	0.160154	0.714636
33	8.037078	0.013952	1027.915	1.5911	0.121645	0.154664	0.723691
34	7.63424	0.013271	1035.549	1.604372	0.118146	0.149416	0.732438

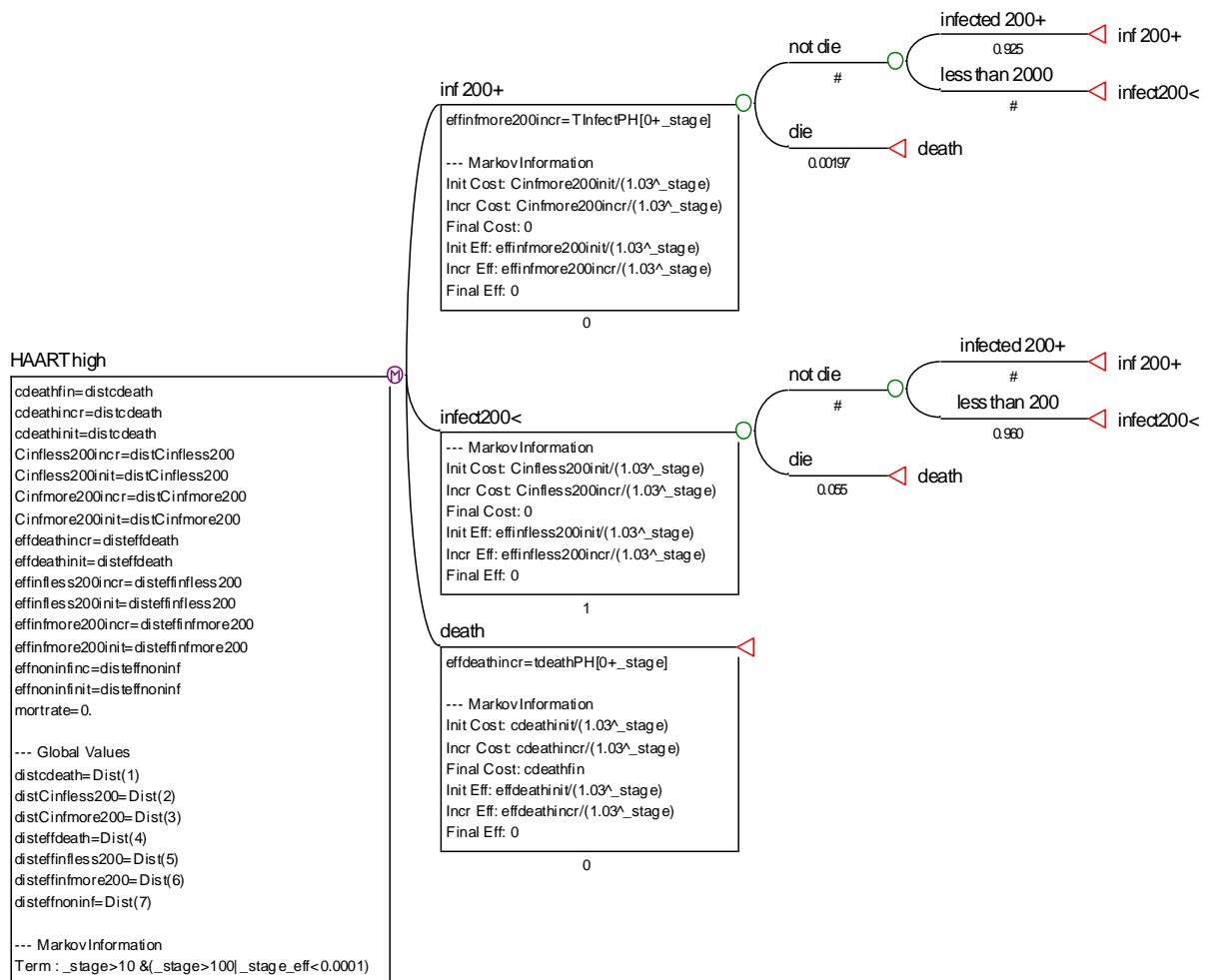
35	7.255077	0.012628	1042.804	1.617	0.114718	0.144394	0.740888
36	6.897874	0.012021	1049.702	1.62902	0.111363	0.139581	0.749056
37	6.561078	0.011446	1056.263	1.640466	0.108084	0.134964	0.756952
38	6.24328	0.010903	1062.506	1.651369	0.104882	0.130529	0.764588
39	5.943195	0.010388	1068.45	1.661757	0.101759	0.126267	0.771974
40	5.659652	0.009901	1074.109	1.671659	0.098715	0.122166	0.779119
41	5.391575	0.00944	1079.501	1.681099	0.095749	0.118218	0.786033
42	5.137979	0.009003	1084.639	1.690102	0.092862	0.114415	0.792723
43	4.897955	0.008589	1089.537	1.698691	0.090053	0.110748	0.799199
44	4.670666	0.008196	1094.207	1.706887	0.087321	0.107211	0.805468
45	4.455336	0.007824	1098.663	1.714711	0.084666	0.103798	0.811536
46	4.251247	0.00747	1102.914	1.722181	0.082085	0.100503	0.817412
47	4.057734	0.007134	1106.972	1.729315	0.079578	0.097321	0.823101
48	3.874176	0.006816	1110.846	1.736131	0.077143	0.094246	0.828611
49	3.699997	0.006513	1114.546	1.742644	0.07478	0.091274	0.833946
50	3.534658	0.006225	1118.081	1.748869	0.072485	0.088401	0.839114
51	3.377657	0.005952	1121.458	1.754822	0.070258	0.085623	0.844118
52	3.228524	0.005692	1124.687	1.760514	0.068097	0.082937	0.848966
53	3.086819	0.005445	1127.774	1.765959	0.066001	0.080337	0.853662
54	2.952132	0.00521	1130.726	1.77117	0.063967	0.077822	0.85821
55	2.824074	0.004987	1133.55	1.776157	0.061995	0.075389	0.862617
56	2.702285	0.004774	1136.252	1.780931	0.060082	0.073033	0.866885
57	2.586423	0.004572	1138.838	1.785502	0.058227	0.070753	0.87102
58	2.476169	0.004379	1141.315	1.789881	0.056428	0.068545	0.875026
59	2.371222	0.004195	1143.686	1.794076	0.054684	0.066408	0.878908
60	2.271298	0.00402	1145.957	1.798096	0.052994	0.064339	0.882668
61	2.176132	0.003853	1148.133	1.80195	0.051355	0.062335	0.886311
62	2.085472	0.003695	1150.219	1.805644	0.049766	0.060394	0.88984
63	1.999082	0.003543	1152.218	1.809187	0.048225	0.058515	0.89326
64	1.916738	0.003399	1154.135	1.812586	0.046732	0.056694	0.896573
65	1.838231	0.003261	1155.973	1.815847	0.045285	0.054931	0.899784
66	1.763362	0.003129	1157.736	1.818976	0.043883	0.053223	0.902894
67	1.691943	0.003004	1159.428	1.82198	0.042524	0.051569	0.905908
68	1.623798	0.002884	1161.052	1.824864	0.041206	0.049966	0.908828
69	1.55876	0.00277	1162.611	1.827633	0.039929	0.048414	0.911657
70	1.496671	0.00266	1164.107	1.830294	0.038692	0.04691	0.914398
71	1.437383	0.002556	1165.545	1.83285	0.037493	0.045453	0.917055
72	1.380754	0.002456	1166.925	1.835306	0.03633	0.044041	0.919628
73	1.326651	0.002361	1168.252	1.837667	0.035204	0.042673	0.922122
74	1.274948	0.00227	1169.527	1.839937	0.034113	0.041348	0.924539
75	1.225527	0.002183	1170.753	1.842119	0.033055	0.040065	0.92688
76	1.178274	0.002099	1171.931	1.844218	0.03203	0.038821	0.929149
77	1.133084	0.002019	1173.064	1.846238	0.031037	0.037616	0.931347
78	1.089855	0.001943	1174.154	1.848181	0.030075	0.036448	0.933477
79	1.048491	0.00187	1175.202	1.850051	0.029142	0.035317	0.935541
80	1.008903	0.0018	1176.211	1.851851	0.028238	0.034221	0.937541

81	0.971004	0.001733	1177.182	1.853584	0.027362	0.033159	0.939479
82	0.934714	0.001669	1178.117	1.855253	0.026514	0.03213	0.941356
83	0.899956	0.001607	1179.017	1.85686	0.025691	0.031133	0.943176
84	0.866657	0.001548	1179.884	1.858409	0.024895	0.030167	0.944939
85	0.834748	0.001492	1180.718	1.8599	0.024122	0.029231	0.946647
86	0.804164	0.001438	1181.522	1.861338	0.023374	0.028324	0.948302
87	0.774842	0.001386	1182.297	1.862724	0.022649	0.027445	0.949906
88	0.746724	0.001336	1183.044	1.864059	0.021947	0.026593	0.95146
89	0.719753	0.001288	1183.764	1.865347	0.021266	0.025768	0.952966
90	0.693878	0.001242	1184.458	1.866589	0.020606	0.024969	0.954425
91	0.669047	0.001198	1185.127	1.867787	0.019967	0.024194	0.955839
92	0.645214	0.001156	1185.772	1.868943	0.019348	0.023443	0.957209
93	0.622332	0.001115	1186.394	1.870057	0.018748	0.022716	0.958536
94	0.600359	0.001076	1186.995	1.871133	0.018166	0.022011	0.959823
95	0.579254	0.001038	1187.574	1.872171	0.017602	0.021328	0.961069
96	0.558978	0.001002	1188.133	1.873174	0.017056	0.020667	0.962277
97	0.539494	0.000967	1188.672	1.874141	0.016527	0.020026	0.963447
98	0.520768	0.000934	1189.193	1.875075	0.016015	0.019404	0.964581
99	0.502765	0.000902	1189.696	1.875977	0.015518	0.018802	0.96568
100	0.485455	0.000871	1190.181	1.876849	0.015036	0.018219	0.966745
101	7.480096	0	1197.661	1.876849	0.01457	0.017654	0.967776

These results were then used to graph how the effectiveness and the cost of each intervention compare in LPC and high Prevalence context. TreeAge pro provides a limited option for graphical analysis of the results. So, I had to export data from TreeAge pro to excel to conduct graphical analysis relevant to the objectives of the study.

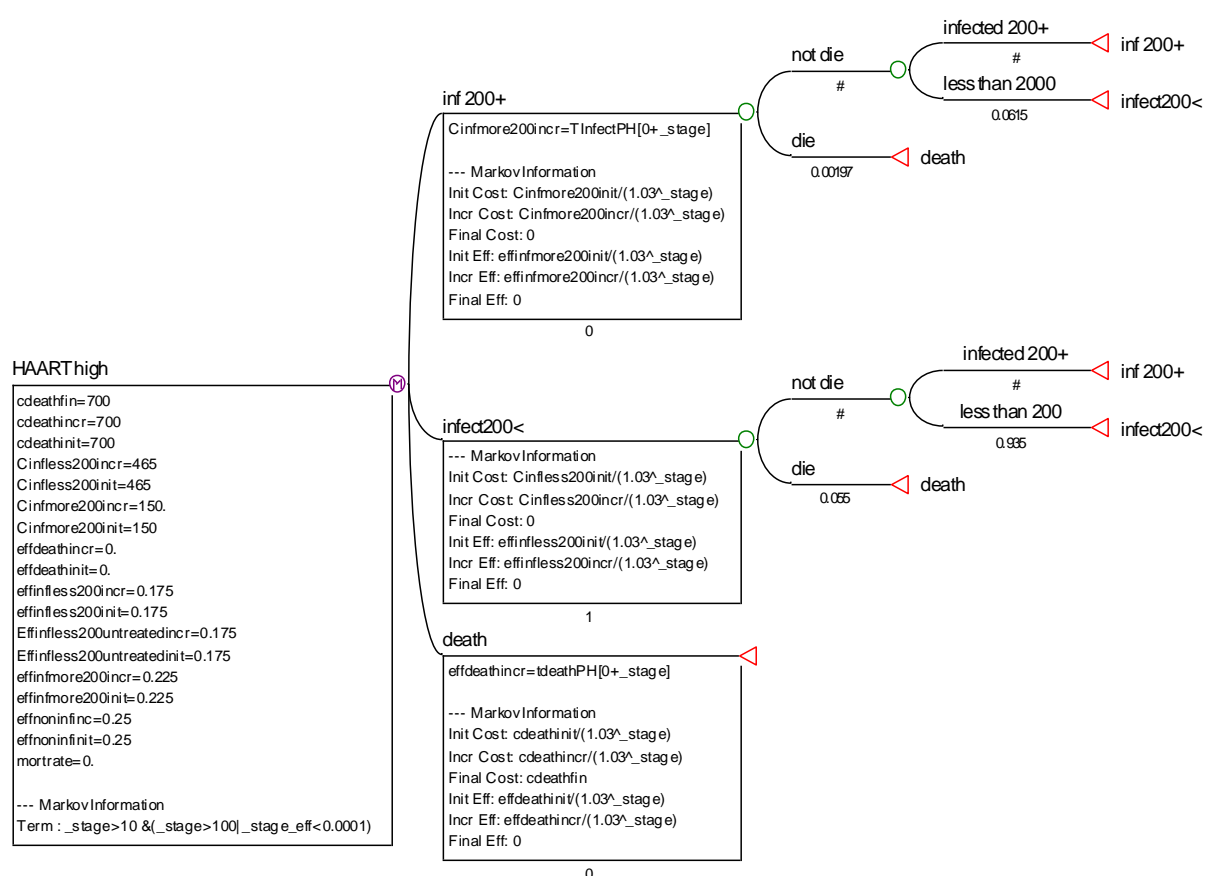
Appendix 17: Markov model structure for HAART intervention with distributions of parameters for probabilistic sensitivity analysis.

To assess the uncertainty of the results, probabilistic sensitivity analysis has to be conducted. This necessitated defining parameter values as distribution rather than variables. With variables transformed into distribution, the evaluation is done thousand times each time picking up a value in the distribution and averaging the 1000 estimates of costs and effectiveness obtained. The figure below shows the structure which includes the distribution of parameters for the sake of probabilistic sensitivity analysis.



Appendix 18: explanation of how a societal perspective was analysed

To analyse the societal perspective, the costs each HIV intervention model was modified to include patients costs. Patients costs consisted of estimates of transport costs to and from facility, waiting time to receive the intervention and funeral costs. These costs are not usually incurred by the government. An example of Markov model structure for HAART intervention in a HPC which takes into consideration societal perspective costs is presented below.



Markov model applies, in each period in an HIV/AIDS state, the cost of the state to patients in that state. In the case of "dead" state, Markov model would apply the cost in the "dead" state to patients in that state. Since, the cost in the "dead" state is once-off cost, and applying the cost at each period implies counting many times the costs in "dead" state for the same patients, the cost in death was adjusted manually in excel. The cost in "dead" state in one period was the cumulative cost in that period minus the cumulative cost in "dead" state in the previous period.

Appendix 19: example of how the number of patients using VCT was estimated.

Province	Estimated population 2010	HCT Target population	Number tested for HIV	% target tested
Eastern Cape	6,884,482	2,737,815	1,267,394	46
Free State	2,972,983	1,479,942	405,399	27
Gauten	9,853,543	5,308,415	1,668,087	31
KZn	10,027,620	4,578,031	2,268,963	50
LM	5,357,949	2,275,491	1,350,641	59
MP	3,646,123	1,660,038	739,226	45
NW	3,229,078	1,537,093	1,109,242	72
NC	1,108,599	485,391	282,211	58
WC	4,945,732	2,203,620	1,481,729	67

Source: SANAC Secretariat (2010)

Estimated the number of patients in each province and found that this number was:

Province	Estimated population 2010	HCT Target population	Annual number	% target tested
Eastern Cape	6,884,482	2,737,815	253,479	0.09
Free State	2,972,983	1,479,942	67,579	0.05
Gauten	9,853,543	5,308,415	278,015	0.05
KZn	10,027,620	4,578,031	378,161	0.08
LM	5,357,949	2,275,491	225,107	0.09
MP	3,646,123	1,660,038	123,204	0.07
NW	3,229,078	1,537,093	184,874	0.12
NC	1,108,599	485,391	47,035	0.10
WC	4,945,732	2,203,620	246,955	0.11

Based on the source of the SANAC secretariat 2010.

Appendix 20: How QALYs in rural context were estimated

The estimation of QALYs required the estimation of quality of life in each Markov states. The study used measure of quality of life from three studies. The Quality of life in AIDS state was assumed to be 0.7 based on the evidence from other studies (Jelsma *et al.*, 2006, O'keefe & Wood (1996), and Louwagie *et al.* (2007). Improvement to Non-aids State was assumed to have 0.84 again based on the values in non-AIDS state in these studies. The study assumed quality of life of 0.90 for non-infected and 0 for the HIV/AIDS "dead" state. The average in O'Keefe was 0.79 for white female and 0.62 for black so $0.62/0.79$ was multiplied to get Quality of life to get a value a rural context and $0.79/0.62$ to get the score in an urban context.

In AIDS in rural context the score was calculated as follows: $62/79 \times 0.7 = 0.55$. The corresponding score in the urban context is $79/63 \times 0.7 = 0.87$. In the non-AIDS we used $62/79 \times 0.84 = 0.67$. In the absence of usual care, we assumed a decrease in the quality of life by 20%. This was a simplistic assumption but probabilistic sensitivity analysis dealt with the potential bias it would bring in the results.

17 March 2014

Mr Josue Mbonigaba (202514748)
School of Accounting, Economics & Finance
Westville Campus

Protocol reference number: HSS/1368/010D

New project title: The cost-effectiveness of HIV/AIDS interventions in South Africa

Dear Mr Mbonigaba,

Approval - Change of project title

I wish to confirm that your application in connection with the above mentioned project has been approved.

Any alteration/s to the approved research protocol i.e. Questionnaire/Interview Schedule, Informed Consent Form, Title of the Project, Location of the Study, Research Approach/Methods must be reviewed and approved through an amendment /modification prior to its implementation. In case you have further queries, please quote the above reference number.

Please note: Research data should be securely stored in the discipline/department for a period of 5 years.

The ethical clearance certificate is only valid for a period of 3 years from the date of issue. Thereafter Recertification must be applied for on an annual basis.

Best wishes for the successful completion of your research protocol.

Yours faithfully



.....
Dr Shenuka Singh (Chair)

/ms

cc Supervisor: Professor Geoff Harris
cc Academic leader Research: Dr C Muller
cc School Administrator: Mr Sihle Khuzwayo

Humanities & Social Sciences Research Ethics Committee

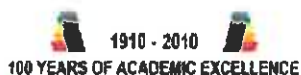
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